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Cost-Effectiveness of 1-Time Universal Screening for Chronic Hepatitis B Infection in Adults in the United States

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Background. An estimated 862 000 to 2.4 million people have chronic hepatitis B infection (CHB). Hepatitis B screening is recommended for pregnant women and populations with increased CHB risk. However, diagnosis rates remain low, with only 33% of people with CHB aware of their infection. This study aimed to assess the cost-effectiveness of universal adult screening for CHB.

Methods. We used a Markov model to calculate the costs, population health impact, and cost-effectiveness of 1-time universal screening and CHB monitoring and treatment compared with current practice. Sensitivity analysis was performed on model parameters to identify thresholds for cost-saving or cost-effectiveness based on a willingness to pay of $50 000/quality-adjusted life-year. The analysis assumed testing would be performed during routine healthcare visits and that generic tenofovir or entecavir would be dispensed for treatment. Testing costs were based on Medicare reimbursement rates.

Results. At an estimated 0.24% prevalence of undiagnosed CHB, universal hepatitis B surface antigen (HBsAg) screening in adults aged 18–69 years is cost-saving compared with current practice if antiviral treatment drug costs remain below $894/year. Compared with current practice, universal screening would avert an additional 7.4 cases of compensated cirrhosis, 3.3 cases of decompensated cirrhosis, 5.5 cases of hepatocellular carcinoma, 1.9 liver transplants, and 10.3 hepatitis B virus–related deaths at a saving of $263 000/100 000 adults screened.

Conclusions. Universal HBsAg screening of adults in the US general population for CHB is cost-effective and likely cost-saving compared with current CHB screening recommendations.

Keywords. universal screening; hepatitis B; antiviral treatment; health policy; cost-saving.

Chronic hepatitis B virus infection (CHB) is a major public health problem. CHB is a silent killer because most people living with CHB are asymptomatic. If left undiagnosed and without care and treatment, 15%–25% will be at risk for premature death from liver cirrhosis, liver failure necessitating liver transplant, or liver cancer [1, 2].

Following the Advisory Committee on Immunization Practices recommendations for universal hepatitis B surface antigen (HBsAg) screening of pregnant women for CHB in 1988 and universal infant hepatitis B immunization in 1991 [3, 4], CHB is currently uncommon in children in the United States. The 2011–2016 National Health and Nutrition Examination Survey (NHANES) reported that there are approximately 840 000–862 000 noninstitutionalized persons in the US population living with CHB, and virtually all of them are adults [5, 6]. CHB prevalences were 0.30%, 0.37%, 0.41%, and 0.35% in persons aged 18–34 years, 35–49 years, 50–64 years, and ≥65 years, respectively [5]. About 30% are US-born [6]. Among US-born adults, non-Hispanic Blacks (0.52%) and Asians (0.79%) have the highest CHB prevalence compared with 0.14% in Mexican Americans and 0.08% in non-Hispanic White Americans [5]. Among non–US-born adults, CHB prevalence among Asians, non-Hispanic Blacks, non-Hispanic Whites, and Mexican Americans was 3.85%, 1.94%, 0.64%, and 0.19%, respectively.

The Centers for Disease Control and Prevention, US Preventive Services Task Force, and American Association for the Study of Liver Diseases recommend universal HBsAg screening of pregnant women for CHB and risk-based hepatitis B testing of nonpregnant, asymptomatic adults including non–US-born adults from endemic countries with HBsAg prevalence ≥2%. However, hepatitis B testing and diagnosis of CHB have remained low [7–9]. According to the recent 2011–2016 NHANES, only an estimated 33% of the US noninstitutionalized population living with CHB in the United States are aware of their infection [6]. Patient-related and healthcare provider or health system–related barriers likely account for low screening and diagnosis rates [10]. Difficulties in implementing testing in primary care settings based on a long list of risk categories and testing based on place of birth from endemic countries when the

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information is not captured in most medical records are often stated as the major obstacles to implementing current testing recommendations by primary healthcare providers [9, 10].

Our aim in this study was to assess the economic and public health impact of a 1-time universal screening of the general adult population for CHB in the United States.

METHODS

Using a Markov model (Supplementary Figure 1), we simulated cohorts' progression through a discrete series of health states. Outcomes in the model included CHB screening, monitoring and treatment costs, quality-adjusted life-years (QALYs), and clinical end points. Results were presented as weighted averages over age and gender where we assumed 50% of the screened population was male, but 58% of those with CHB were male. We computed results for a hypothetical population of 100 000 men and women aged 18–69 years to potentially be screened. We ran a lifetime analysis. Key input variables and ranges are shown in Table 1.

Population Prevalence Calculation

The prevalence of HBsAg in the United States was based on the 2011–2016 NHANES that reported HBsAg prevalence was 0.36% among adults aged ≥18 years, 58% were male, and 67% were unaware of their infection [6]. We multiplied 0.36% by 67% to obtain an estimated prevalence of 0.24% undiagnosed CHB, which we used as our base case prevalence. We also varied the undiagnosed HBsAg prevalence in a sensitivity analysis.

Disease Progression and Treatment-Related Estimates

The natural history of CHB and disease progression rates were derived from recent cohort studies and meta-analyses mainly from North America for hepatitis B virus (HBV) monoinfected patients (Supplementary Table 2A) [11–21]. A 50% reduction in disease progression estimates was applied for females based on recent gender-specific studies [22–24]. Treatment effectiveness estimates were expressed as reductions in disease progression risks for treatment-naive patients (Supplementary Table 2B) [25–30]. We assumed effective antiviral suppression would reduce liver cancer risks in cirrhotic and noncirrhotic patients by 50% and 70%, respectively, compared with natural history [27, 28, 30]. Disease progression between health states, conditional on treatment, age (where available), and gender, was simulated in 1-year cycles. Causes of death that were not related to CHB were included in the model based on age-specific mortality rates from life tables in the National Statistics Report [31].

Model

A Markov model was developed using TreeAge Pro 2020 to simulate long-term outcomes, including cirrhosis, decompensated cirrhosis, hepatocellular carcinoma (HCC), and CHB-related death (Supplementary Figure 1). Without screening and treatment, patients follow the disease natural history. The proportion of patients in each disease state depends on the rates of screening and treatment evaluated in each scenario. Those in the inactive CHB health state are those who are HBsAg-positive with normal alanine aminotransferase (ALT) levels and no cirrhosis. Those with cirrhosis or active disease would be candidates for treatment. Following the recent 2018 American Association for the Study of Liver Diseases (AASLD) guidelines [32], active hepatitis where treatment is indicated is defined by an elevation of ALT ≥2 upper limits of normal or evidence of significant fibrosis (≥F2) associated with ALT above the upper limit of normal plus elevated HBV DNA above 2000 IU/mL for hepatitis B e antigen (HBeAg)-negative and above 20 000 IU/mL for HBeAg-positive individuals. Annual probabilities of receiving a liver transplant for CHB-related decompensated cirrhosis and HCC (1.2% and 7%, respectively) were calculated based on data from the Organ Procurement and Transplantation Network [33]. If progression rates were reported, these were transformed into annual probabilities using a standard formula ($P = 1 - e^{-rt}$) where P is the probability and r is the annualized progression rate.

Scenarios

We considered 2 scenarios: current practice vs current practice plus 1-time universal hepatitis B screening. Current practice was adapted from Harris et al [7]. We assumed 33% of people are currently diagnosed [6], 36% are linked to care, and 18% of those diagnosed are receiving treatment [7]. In the model, current practice did not distinguish subsets of risk-based population from the general population screened. In our base case, we assumed adherence to treatment is 90% among patients without cirrhosis and 100% among patients with cirrhosis [34]. We assumed entecavir (ETV) and tenofovir, the highly potent and low-risk-for-drug-resistance antiviral medications, had similar efficacy and that all patients received lifetime treatment with commonly prescribed generic ETV or generic tenofovir disoproxil fumarate (TDF; Table 1).

Costs and Utilities

The cost of HBsAg testing was based on a Medicare reimbursement of $10.33. Although the lowest price for antiviral drugs is generic TDF at $325 per year [35], we used an annual antiviral drug cost of $502 with the assumption that 60% of the patients will be dispensed generic TDF and 40% generic ETV [7]. We obtained other medical management costs for CHB, cirrhosis, decompensated cirrhosis, and liver cancer from Liu et al [36]. Medical management costs were adjusted for inflation using the US consumer price index to reflect 2020 dollars [37]. For patients diagnosed with CHB and linked to care, we assumed that they will receive initial baseline tests (HBeAg, complete blood count, liver function tests, HBV DNA), have twice yearly clinic visits with ALT blood tests, and receive

Table 1. Key Input Variables and Ranges

Variable	Base Case	Range	Reference
Age/birth cohort, years	≥18	18–69	
HBsAg prevalence in US adult population, %	0.36	0.29–0.46	Patel et al 2019 [6]
Male-to-female ratio of positive HBsAg population	58:42		Patel et al 2019 [6]
Percent not aware of their infection	67		Patel et al 2019 [6]
Estimated prevalence of undiagnosed US adult population who are HBsAg-positive, %	0.24		
Percent adults diagnosed with CHB and linked to care and received antiviral treatment	18	17–19	Harris et al 2020 [7]
Percent adults with cirrhosis diagnosed with CHB who are linked to care and receive antiviral treatment	100		Assumption
Percent adults who are eligible for treatment	30	26–30	Kim et al, Moorman et al, Nguyen et al, Toy et al [41–44]
Screening Costs, $			
Cost of hepatitis B serologic tests			
HBsAg	$10.33		Medicare reimbursement
Hepatitis B core antibody	$10.74		Medicare reimbursement
Hepatitis B surface antibody	$12.05		Medicare reimbursement
All 3 hepatitis B tests	$28.27		Medicare reimbursement
Linkage to care and treatment costs			
Antiviral drug costs per year[a]	$502	$326–$16 464[b]	Redbook (22 January 2021) [35]
Initial baseline tests (hepatitis B e antigen, complete blood count, liver function tests, HBV DNA)	$86.74	$43.23–$129.71	Medicare reimbursement
Total annual monitoring costs[c]	$369	$185–$554	Medicare reimbursement
Clinic visit × 2	$74 × 2	$37–$111	Medicare reimbursement
Ultrasound × 1 (50% none, 50% × 2)	$125 × 1	$62–$187	Medicare reimbursement
Alpha fetoprotein × 2 (50% none, 50% × 2)	$23 × 2	$12–$35	Medicare reimbursement
Alanine aminotransferase × 2	$7 × 2	$4–$11	Medicare reimbursement
HBV DNA × 1	$59 × 1	$29–$88	Medicare reimbursement
Annual disease management costs[d]			
CHB	$1695	$176–$6808	Liu et al 2012 [36]
Cirrhosis	$5045	$176–$6181	Liu et al 2012 [36]
Decompensated cirrhosis	$13 362	$4269–$32 299	Liu et al 2012 [36]
Hepatocellular carcinoma	$53 197	$25 654–$76 954	Liu et al 2012 [36]
Liver transplantation first year	$182 004	$145 603–$218 405	Liu et al 2012 [36]
Liver transplantation second year	$26 085	$20 868–$31 302	Liu et al 2012 [36]
Health state utilities			
Active CHB	0.91	(0.80–0.92)	Woo et al (EQ-5D) [40]
Cirrhosis	0.88	(0.78–0.88)	Woo et al (EQ-5D) [40]
Inactive CHB	1.00	(0.90–1.00	Assumption
Decompensated cirrhosis	0.73	(0.49–0.82)	Woo et al (EQ-5D) [40]
Hepatocellular carcinoma	0.81	(0.77–0.85)	Woo et al (EQ-5D) [40]
Liver transplantation	0.84	(0.72–0.84)	Woo et al (EQ-5D) [40]
HBsAg seroclearance	1.00	(0.95–1.00)	Assumption
Viral suppression	1.00	(0.95–1.00)	Assumption

Abbreviations: CHB, chronic hepatitis B; EQ-5D, EuroQoL 5D; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.

[a]Assuming 60% on generic tenofovir disoproxil fumarate and 40% on generic entecavir [7].

[b]This is the range for 1-way sensitivity analysis; however, for the probabilistic sensitivity analysis, it varies from $326 to $1460.

[c]Annual monitoring is the total cost including biannual clinic visits and blood tests for alanine aminotransferase and annual HBV DNA level plus assuming 50% would receive additional hepatocellular carcinoma surveillance consisting of biannual liver ultrasound and alpha fetoprotein blood tests as recommended by the American Association for the Study of Liver Diseases [38].

[d]Adjusted to 2020 dollars using the 2020 Medical Consumer Price Index [37].

yearly HBV DNA level tests and that eligible patients (50%) would receive additional HCC surveillance consisting of liver ultrasound and alpha fetoprotein every 6 months as recommended by AASLD [38] (Table 1). Costs of testing and clinic visits were based on Medicare reimbursement rates [39] (Table 1). We assumed patients who achieved HBsAg loss would continue to incur annual costs for long-term CHB monitoring. All costs and QALYs were discounted at a rate of 3% per year. The analysis was performed from the healthcare system perspective. We used EQ5D utility assessments calculated by Woo et al

[40] based on a Canadian CHB patient sample and included age adjustments.

Outcomes

We validated the disease model by comparing HBV-related and overall survival to a natural history cohort [45] and cumulative cirrhosis incidence in a cohort with active CHB [46] (Supplementary Figure 2A–C). Outcomes included lifetime costs, QALYs, and clinical end points. We calculated the incremental cost-effectiveness ratio (ICER) comparing the incremental costs of universal screening compared with current practice divided by the incremental QALYs gained from screening vs current practice. We used the $50 000 per QALY threshold as a cutoff to identify cost-effective interventions [47].

Sensitivity Analyses

We used 1-way sensitivity analysis to determine the parameters that had the greatest impact on the results. We also conducted a probabilistic sensitivity analysis varying all parameter values across reasonable distributions to evaluate the impact of overall parameter uncertainty on outcomes.

RESULTS

The health economic model showed cost-saving and better health outcomes when comparing 1-time universal HBsAg testing plus current practice compared with current practice alone (Table 2). Compared with current practice, universal screening would avert an additional 7.4 cases of compensated cirrhosis, 3.3 cases of decompensated cirrhosis, 5.5 cases of HCC, 1.9 liver transplants, and 10.3 HBV-related deaths per 100 000 people aged 18–69 years screened. Universal HBsAg screening would save $262 857 and would result in a gain of 135 QALYs per 100 000 adults screened.

Sensitivity Analyses

Cost-effectiveness of universal screening was sensitive to a small number of parameters. Supplementary Figure 3 shows the results of 1-way sensitivity analyses summarized using a tornado plot, and Supplementary Table 3 shows the 1-way sensitivity analysis results for all parameters. If the average annual antiviral drug cost was ≥$9692/year, then universal screening would not be cost-effective (Figure 1). If the annual antiviral treatment drug cost was <$894/year, then universal HBsAg screening for CHB would remain cost-saving. The prevalence of undiagnosed CHB and cost of hepatitis B testing were the next most important parameters, but they did not increase the ICER above $50 000/QALY (Table 3). Undiagnosed HBsAg prevalence needed to fall to very low levels (<0.026%) in order for universal screening to no longer be cost-effective (Table 3, Supplementary Figure 4).

Next, we examined how HBsAg prevalence and cost of hepatitis B testing together might affect the cost-effectiveness of testing (Figure 2). At the current undiagnosed CHB prevalence of 0.24%, if the HBsAg screening test cost was higher at $12.96 instead of $10.33, then universal screening would be cost-effective but no longer cost-saving. At the current Medicare reimbursement of $28.27, universal screening with a 3-test panel for past and current hepatitis infection and immunity (HBsAg, hepatitis B core antibody [anti-HBc], and hepatitis B surface antibody [anti-HBs]) would be cost-effective with an ICER of $11 207/QALY. If undiagnosed prevalence was slightly lower at 0.19% instead of the base case of 0.24%, then universal HBsAg screening would be at the threshold between cost-saving and cost-effective.

To assess the impact of universal screening coupled with an increase in the CHB treatment rate, we found that if the treatment rate increased from the base case of 18% to 25%, it would result in higher cost-saving (saving of $1 069 905), further reduction in cases of cirrhosis (14.3), HCC (9.7), liver transplants (3.3), and death (17.7), and higher QALYs gained (228) (Supplementary Table 4). If the treatment adherence rate dropped to 75%, universal screening would remain cost-effective at $298/QALY (Supplementary Table 5).

The probabilistic sensitivity analysis that varies all parameters simultaneously shows a >99% likelihood that universal screening would be cost-effective at a willingness to pay of $50 000/QALY (Figure 3).

DISCUSSION

CHB remains a major global public health problem. In 2015, the World Health Organization (WHO) estimated that there were 257 million people living with CHB in the world and 887 000 HBV-related deaths largely from cirrhosis and liver cancer caused by CHB [48]. Most of the deaths associated with

Table 2. Clinical Outcome and Cost-Effectiveness of 1-Time Universal Hepatitis B Surface Antigen Screening for Chronic Hepatitis B Compared With Current Practice for a Population of 100 000 Persons Aged 18–69 Years

Scenarios	Cirrhosis	Decompensated Cirrhosis	Hepatocellular Carcinoma	Transplants	Hepatitis B Virus Deaths	Cost[a]	Quality-Adjusted Life-Years	Incremental Cost-Effectiveness Ratio
CP	24.9	7.6	23.9	8.0	38.0	8 747 703	2 062 384	-
CP + 1-time universal screening	17.5	4.3	18.4	6.1	27.7	8 484 846	2 062 521	-
Difference	–7.4	–3.3	–5.5	–1.9	–10.3	–262 857	+137	Cost-saving

Abbreviation: CP, current practice.

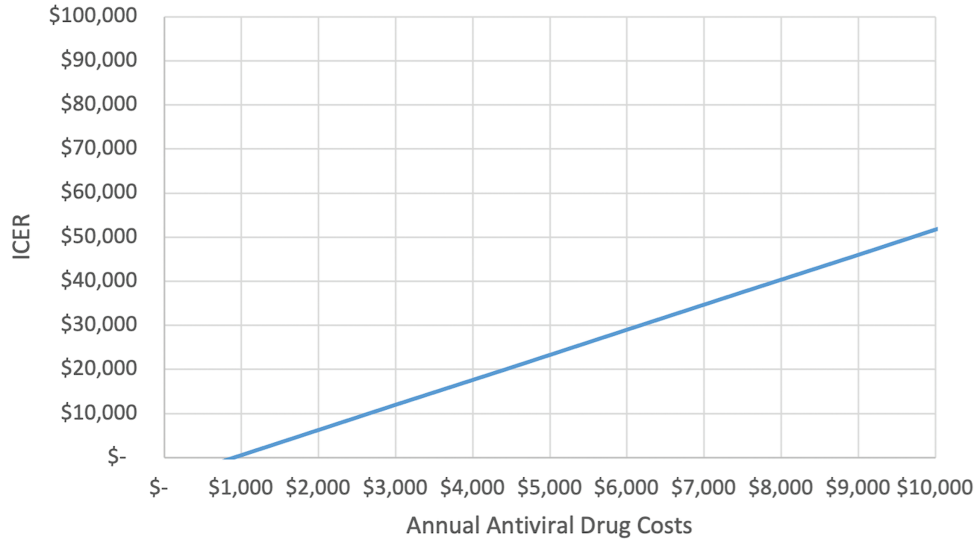

Figure 1. Sensitivity analysis on annual antiviral treatment drug costs on cost-effectiveness of chronic hepatitis B screening. Willingness to pay or ICER threshold of $50 000/quality-adjusted life-year is considered cost-effective. Abbreviation: ICER, incremental cost-effectiveness ratio.

CHB could be averted through diagnosis, monitoring, and antiviral treatment to prevent hepatic inflammation and prevent or reverse liver fibrosis. However, among those living with CHB, diagnosis and treatment rates were less than 10% worldwide in 2015. In response to the United Nations 2030 Sustainable Development Goal to combat viral hepatitis, the WHO global hepatitis elimination strategy, endorsed in 2016 by all member countries, set a 2030 target to increase CHB diagnosis and eligible treatment rates to 90% and 80%, respectively, in order to reduce HBV-related deaths [48].

Table 3. Incremental Cost-Effectiveness Ratio for 1-Time Universal Hepatitis B Screening Compared With Current Practice by Various Undiagnosed Chronic Hepatitis B Prevalence Points and Testing Costs

Undiagnosed Chronic Hepatitis B Prevalence, %	Base Case Incremental Cost-Effectiveness Ratio (Hepatitis B Surface Antigen Test at $10.33)	Cost-Saving (Testing Costs Threshold)	Cost-Effective at $50 000/Quality-Adjusted Life-Years (Testing Costs Threshold)
0.01	$171 971	$0.54	$3.39
0.02	$81 243	$1.08	$6.77
0.03	$51 001	$1.62	$10.16
0.04	$35 879	$2.16	$13.55
0.05	$26 807	$2.70	$16.93
0.10	$8661	$5.40	$33.86
0.15	$2613	$8.10	$50.80
0.20	Cost-saving	$10.80	$67.73
0.25	Cost-saving	$13.50	$84.66
0.30	Cost-saving	$16.20	$101.59
0.40	Cost-saving	$21.60	$135.45
0.50	Cost-saving	$27.00	$169.32

Base cost of the hepatitis B surface antigen screening test is $10.33.

CHB is recognized in the United States as a major public health problem [1]. Based on the 2011–2016 NHANES, there are approximately 840 000–862 000 noninstitutionalized persons in the US population living with CHB, although by some estimates the number could be as high as 2.4 million [5, 6, 49–51]. In 2018, there were 1649 HBV-related deaths reported on death certificates, although the actual number of HBV-related deaths could be 5 times higher [52]. The Chronic Hepatitis B Cohort Study reported only 19% of CHB decedents, and 40% of those dying from liver disease had hepatitis B reported on their death certificates. CHB patients also died at an average age of 59.8 years, which is 14 years younger than the general US population [52]. Cirrhosis and liver cancer caused by CHB is the fourth leading cause of liver disease for liver transplantation in adults, accounting for about 550 liver transplants each year [53]. The National Academies of Sciences, Engineering, and Medicine concluded that eliminating the public health problem of chronic hepatitis B in the United States is feasible with increased testing and treatment of CHB, elimination of perinatal transmission, and vaccination of infants and adults at increased risk of infection [49]. Achieving the WHO 2030 CHB diagnosis and treatment targets in the United States could reduce HBV-related deaths by 37%–49% and would likely be highly cost-effective and even cost-saving [54].

This analysis suggests a 1-time universal screening of the US population aged 18–69 years for CHB is likely cost-saving and would result in better health outcomes with reduction in cases of cirrhosis, decompensated cirrhosis, HCC, liver transplants, and HBV-related deaths (Table 2, Supplementary Table 6). Current CHB testing recommendations that are based on whether persons are non–US-born from endemic countries with HBsAg prevalence of ≥2% and based on a long list of risks

Figure 2. Sensitivity analysis on undiagnosed CHB prevalence and hepatitis B testing costs on cost-effectiveness of CHB screening. Willingness to pay or incremental cost-effectiveness ratio threshold of $50 000/quality-adjusted life-year is considered cost-effective. Abbreviation: CHB, chronic hepatitis B.

categories are difficult in practice to implement by primary healthcare providers because risk factors including country of birth and whether the patient is an immigrant are not collected by the health system. As a result and despite screening being covered by the Affordable Care Act and Centers for Medicare and Medicaid Services as a routine preventive service, current testing recommendations have not led to significant increases in hepatitis B testing, diagnosis, and treatment. A national recommendation for universal CHB screening beyond pregnant women will greatly simplify the screening process and can be readily included in the electronic medical records system to offer all adults a 1-time hepatitis B test. In the national strategy for the elimination of hepatitis B and C report, the National Academies recommended that the National Committee for Quality Assurance establish Healthcare Effectiveness Data and Information Set (HEDIS) measures to compel providers and health plan managers to comply with viral hepatitis screening guidelines [49]. Universal CHB screening of adults beyond

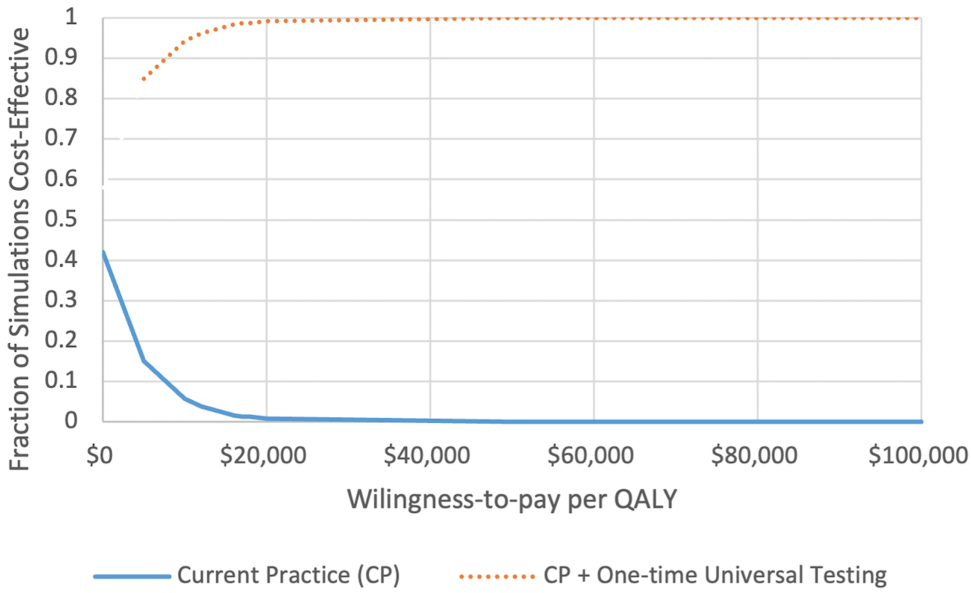

Figure 3. Cost-effectiveness acceptability curves. Abbreviation: QALY, quality-adjusted life-year.

pregnant women rather than risk-based testing would make such a recommendation for compliance monitoring feasible.

We found that universal screening of adults aged 18–69 years at the estimated undiagnosed HBsAg prevalence rate of 0.24% is likely cost-saving or highly cost-effective. In the unlikely event that the undiagnosed prevalence is very low (<0.026%) or the average annual antiviral treatment drug cost is very high (≥$9692 per year), then universal screening would no longer be cost-effective. However, 0.026% prevalence is 9 times lower than our current estimate of undiagnosed CHB in the general population. Moreover, an annual average antiviral drug cost of $9692/year is more than 10 times higher than the costs of generic ETV and tenofovir, meaning most patients would be receiving the expensive branded antiviral medications.

This analysis does have some limitations. We assumed screening would be performed as part of regular visits to healthcare providers. We did not include costs associated with a separate clinic visit for hepatitis B screening or other programmatic costs such as outreach and education. Our sensitivity analysis on the cost of screening can be used to evaluate increased screening costs. We assumed screening for CHB would be similar to the recommendation for pregnant women with HBsAg [55]. The addition of anti-HBs and anti-HBc testing would have the added benefit of helping to determine if the person is immune or would benefit from vaccination, but we did not examine vaccination policies for this analysis. Hepatitis B testing that included the 3 tests (HBsAg, anti-HBs, and anti-HBc) would add costs to a universal CHB screening strategy. However, at a Medicare reimbursement cost of $28.27 for all 3 tests, our analysis found it would be cost-effective at $11 207/QALY. In our sensitivity analysis, we found that universal screening would remain cost-effective if screening and programmatic costs were less than $81.27 per person. It is estimated that 20%–40% of patients with CHB should be treated with antiviral therapy [7, 48]. In this analysis, we assumed among persons diagnosed with CHB, currently in the United States only 18% received treatment [7]. We also assumed patients without cirrhosis were only 90% adherent to treatment [56]. Sensitivity analyses showed that if the treatment rate further increases, it would result in incremental health benefits and cost-saving (Supplementary Table 4). Drug prices were based on Redbook, although lower discounted prices were listed by some major pharmacy chains. Our analysis did not take into consideration patients living with human immunodeficiency virus, hepatitis C virus, or hepatitis delta virus coinfection.

In 2011, Eckman et al suggested that screening and treatment of CHB with a low-cost, high-resistance nucleoside and nucleotide antiviral was cost-effective at $29 230/QALY in populations with prevalence as low as 0.3% [57]. Since that time, drug costs for first-line highly effective and low-risk-for-drug-resistance antivirals, TDF and ETV, have dropped by more than 20-fold following the introduction of generic TDF and ETV. In our analysis, we found that universal HBsAg screening of adults in the US general population for CHB and treatment with generic TDF and ETV are cost-effective and likely cost-saving at the current estimated undiagnosed HBsAg prevalence of 0.24%. From a public health perspective, 1-time universal screening of adults for CHB would prevent an additional 23 000 deaths from CHB-related liver disease and liver cancer at an estimated cost-saving of $596 000 000 (Supplementary Table 6). If the prevalence of CHB in the United States is 2–3 times higher than the NHANES estimate as several studies have reported [48–51], as many as 45 000–68 000 deaths could be averted with trillions of dollars in cost-saving.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Disclaimer. The findings and conclusions presented here are those of the authors and do not necessarily reflect the official position of the Centers for Disease Control and Prevention (CDC) or the authors' affiliated institutions.

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