**Technical Appendix**

**Cost-Effectiveness of Hepatitis B Screening and Vaccination at Sexually Transmitted Infection Clinics**

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# Figure 1. Markov Schematic



# Figure 2. Scenarios (A) Status Quo, (B) HBsAg only, (C) HBsAg and anti-HBs, (D) HBsAg and anti-HBs and anti-HBc

A

B

C

D

# Additional Methodological Detail on vaccination rates/completion:

We use Miriti’s (4) data on the fraction of individuals at an STI clinic that would receive their first dose of the HBV vaccine: 74%. We then use data from Bruxvoort (53) on completion of the vaccine series. Bruxvoort et al. is a study from a large health system that tracks completion of the 2-dose and 3-dose HBV vaccine series in an integrated health care organization. The figure in that paper shows that completion of the second dose of the three-dose vaccine is almost identical to completion of the second dose of the two-dose vaccine. The authors report 60.5% of people completed two doses 1 year after the first dose and 32.3 completed three doses 1 year after the first dose. The table below shows the absolute percentage of the population receiving exactly 1, 2, or 3 doses of vaccine under a 2-dose or 3-dose vaccination policy. Recall that the assumptions of those receiving the 2nd and 3rd doses are contingent upon receiving the 1st dose.

# Appendix Table 1: Vaccination Rate Assumptions and Calculations

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Vaccination Completion** |   |  |  |   |
| **Assumptions** | **Parameter Assumption** | **Range** | **Distribution\*** | **Source** |
| Fraction receiving 1st dose | 74% | (67%-81%) | beta | Miriti, 2008 (4) |
| Fraction receiving 2nd dose (of those receiving 1st dose) | 60.5% | (47.7%-62.7%) | beta | Bruxvoort, 2020 (53) |
| Fraction receiving 3rd dose (of those receiving 1st dose) | 32.3% | (27%-33%) | beta | Bruxvoort, 2020 (53) |
| **Resulting Exact Fraction of the Population Vaccinated** | **Calculated Value** |  |  | **Formula** |
| **2-dose vaccine policy** |  |  |  |  |
| **Exactly 1 dose** | 29.2% |  |  | 74% x (1-60.5%) |
| **Exactly 2 doses** | 44.8% |  |  | 74% x 60.5% |
| **3-dose vaccine policy** |  |  |  |  |
| **Exactly 1 dose** | 29.2% |  |  | 74% x (1-60.5%) |
| **Exactly 2 doses** | 20.9% |  |  | 74% x (60.5%-32.3%) |
| **Exactly 3 doses** | 23.9% |  |  | 74% x 32.3% |

\* These are the distributions used for the probabilistic sensitivity analysis. The distributions are set such that the means are centered on the base-case value and the standard deviations of the distributions are set to match one quarter of the ranges specified in the “Range” column of this table. Parameters with no distribution identified were not varied in probabilistic sensitivity analysis. More details are described further on in the Appendix.

# Appendix Table 2. Transition estimates acute infection

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Acute Infection** |  Base Case |  Range | Distribution\* |  Reference |
| Acute hepatitis |  |  |  |  (13) |
| To Symptomatic | 0.3 | 0.20-0.40 | beta |   |
| To Asymptomatic | 1- symptomatic |  |  |   |
| **Acute hepatitis symptomatic** |   |   |  |   |
| To Hospitalized | .12 | .02-.5 | beta | Hutton |
| To fulminant hepatitis | 0.04 | 0.03-0.05 | beta |  (13) |
| To HBsAg+ active CHB no cirr | 0.05 | 0.01-0.10 | beta |  (13) |
| To HBsAg clearance | 1-HBeAg+active CHB |  |   |
| **Acute hepatitis asymptomatic** |   |   |  |   |
| To HBeAg+ Active CHB no cirr | 0.05 | 0.01-0.10 | beta |  (13) |
| To HBsAg clearance | 1- HBeAg+active CHB |  |   |
| **Fulminant hepatitis**  |   |   |  |   |
| To HBeAg+ Active CHB no cirr | 0.071 | 0.053-0.089 | beta |  (13) |
| To HBsAg clearance | 1- HBeAg+active CHB |  |   |
| To liver transplant | 0.017 | 0.0169-0.045 | beta |  (13) |
| To HBV death | 0.67 | 0.503-0.838 | beta |  (13) |

\* These are the distributions used for the probabilistic sensitivity analysis. The distributions are set such that the means are centered on the base-case value and the standard deviations of the distributions are set to match one quarter of the ranges specified in the “Range” column of this table. Parameters with no distribution identified were not varied in probabilistic sensitivity analysis. More details are described further on in the Appendix.

# Appendix Table 3. Natural history chronic hepatitis transition estimates

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Transition (per year)** | **Natural History Estimate** | **Range** | **Distribution\*** | **Reference** |
| **From Active CHB HBeAg-positive** |  |  |  |  |
| HBsAg loss | 0.60% | (0.30%-0.90%) | beta | (25) |
| To Cirrhosis | 1.60% | (1.30%-1.90%) | beta | (53) |
| To HCC | 1.47% | (0.40%-2.55%) | beta | (16) |
|  To HBV-related Death | 0.11% | (0.09%-0.14%) | beta | (16) |
| Inactive | 7.0% | (4.0%-10.0%) | beta | (19) |
| **From Active CHB HBeAg-negative** |  |  |  |  |
| HBsAg loss | 0.60% | (0.30%-0.90%) | beta | (25) |
| To Active HBeAg-positive (reversion) | 0.16% | (0.08%-0.24%) | beta | (15, 54, 55) |
| To Cirrhosis | 2.80% | (1.30%-4.30%) | beta | (53) |
| To HCC | 0.72% | (0.21%-1.23%) | beta | (16) |
| To HBV-related Death | 0.11% | (0.09%-0.14%) | beta | (16) |
| Inactive | 1.60% | (0.00%-6.00%) | beta | (19) |
| **From Compensated Cirrhosis** |  |  |  |  |
| To HBsAg loss | 0.6% | (0.3%-0.9%) | beta | (25) |
| To Decompensated Cirrhosis | 3.90% | (1.95%-5.85%) | beta | (18) |
| To HCC | 3.16% | (2.58%-3.74%) | beta | (16) |
| To HBV-related Death | 4.89% | (3.16%-6.63%) | beta | (16) |
| To Viral Suppression | 6.30% | (3.15%-9.45%) | beta | (23) |
| **From Decompensated Cirrhosis** |  |  |  |  |
| To Liver Transplantation | 1.2% | (1.0%-3.0%) | beta | (56) |
| To HCC | 7.10% | (3.55%-10.65%) | beta | (18) |
| To HBV-related Death | 15.0% | (7.5%-22.5%) | beta | (18) |
| **From HCC** |  |  |  |  |
| To Liver Transplantation | 7.0% | (5.0%-9.0%) | beta | (56) |
| To HBV-related Death  | 15.10% | (13.9%-16.4%) | beta | (16) |
| **From Viral Suppression Cirrhosis** |  |  |  |  |
| HBsAg loss | 1.0% | (0.5%-1.5%) | beta | (25) |
| To HCC | 1.58% | (1.29%-1.87%) | beta | (16) |
| To HBV-related Death | 2.44% | (1.58%-3.31%) | beta | (16) |
| **From Liver Transplantation Decompensated Cirrhosis** |  |  |  |  |
| To HBV-related death year 1 | 17.0% | (8.5%-48.0%) | beta | (24) |
| To HBV-related death year 2+ | 2.50% | (1.25%-24.00%) | beta | (24) |
| **From Liver Transplantation HCC** |  |  |  |  |
| To HBV-related death year 1 | 16% | (8%-48%) | beta | (24) |
| To HBV-related death year 2+ | 2% | (2%-25%) | beta | (24) |
| Relative risk of death after liver transplant (used only for sensitivity analysis and applied to all liver transplantation states) | 1.0 | (0.5-1.5) | beta | assumption |
| **From Inactive**  |  |  |  |  |
| To HBsAg loss |  |  |  |  |
| Age-Group 40-49 | 1.65% | (0.82%-2.47%) | beta | (21, 22) |
| Age-Group 50+ | 1.80% | (0.91%-2.74%) | beta | (21, 22) |
| To active CHB, HBeAg-negative |  |  |  |  |
| Age-Group 40-49 | 2.80% | (1.4%-4.1%) | beta | (21, 22) |
| Age-Group 50+ | 2.00% | (1.0%-3.0%) | beta | (21, 22) |
| To Cirrhosis |  |  |  |  |
| Age-Group 40-49 | 0.07% | (0.034%-0.102%) | beta | (21, 22) |
| Age-Group 50+ | 0.15% | (0.052%-0.202%) | beta | (21, 22) |
| To HCC | 0.17% | (0.02%-0.62%) | beta | (17) |
| **From HBsAg loss**  |  |  |  |  |
| To Cirrhosis | 0.28% | (0.14%-0.42%) | beta | (21, 22) |
| To HCC | 0.09% | (0.045%-0.136%) | beta | (57) |
| **Gender** |  |  |  |  |
| Relative Progression Rates for females† | 0.5 | (0.25-1.0) | beta | (27, 28, 58) |
| Fraction of chronic HBV cases that are Male | 65% | (50%-80%) | beta | (2) |

\* These are the distributions used for the probabilistic sensitivity analysis. The distributions are set such that the means are centered on the base-case value and the standard deviations of the distributions are set to match one quarter of the ranges specified in the “Range” column of this table. Parameters with no distribution identified were not varied in probabilistic sensitivity analysis. More details are described further on in the Appendix.

† A 50% reduction in disease progression estimates was applied for females

Abbreviations: CHB, chronic hepatitis B; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma

# Appendix Table 4. Treatment transition estimates

|  |  |  |  |
| --- | --- | --- | --- |
| **Transition (per year)** | **Treatment Estimate** | **Range** | **Reference** |
| **From Active CHB HBeAg-positive** |  |  |  |
| HBsAg loss | 3% | (1.5-4.5) | (42) |
| To Cirrhosis | 0 | 0 |  assumption |
|
| To HCC | 0.44% | (0.12-0.765) |  (70% reduction)(31, 32) |
|
| To HBV-related Death | 0 | 0 |  assumption |
| To Drug Resistance | 0.01% | (0.0-0.01) | (29, 30, 33) |
| To Viral Suppression  | 76% | (65.0-85.0) | (42) |
| **From Active CHB HBeAg-negative** |  |  |  |
| HBsAg loss | 1% | (0.5-1.5) | (42) |
| To Cirrhosis | 0 | 0 | assumption |
| To HCC | 0.22% | (0.063-0.369) |  (70% reduction)(31, 32) |
|
| To HBV-related Death | 0 | 0 |  assumption |
| To Drug Resistance | 0.01% | (0.0-0.01) | (29, 30, 33) |
| To Viral Suppression  | 93% | (65.0-99.0) | (42) |
| **From Compensated Cirrhosis** |  |  |  |
| To HBsAg loss | 1.70% | (0.85-2.55) | (59) |
| To Decompensated Cirrhosis | 1.80% | (0.90-2.70) | (50% reduction)  |
| To HCC | 1.60% | (1.25-1.75) | (50% reduction) (34) |
| To HBV-related Death | 2.40% | (1.58-3.30) | (50% reduction)  |
| To Viral Suppression | 78% | (65.0-78.0) | (34) |
| To Drug Resistance | 0.01% | (0.0-0.01) | (29, 30, 33) |
| **From Decompensated Cirrhosis** |  |  |  |
| To Liver Transplantation | 1.20% | (0.60-1.80) | (56) |
| To HCC | 3.50% | (1.75-5.25) | (50% reduction) (34) |
|
| To HBV-related Death | 7.50% | (3.75-11.25) | (50% reduction)  |
| To Viral Suppression | 78% | (65.0-78.0) | (34) |
| To Drug Resistance | 0.01% | (0.0-0.01) | (29, 30, 33) |
| **From HCC** |  |  |  |
| To Liver Transplantation | 7% | (5.0-9.0) | (56) |
| To HBV-related Death  | 15.10% | (13.9-16.4) | (34) |
| **From Viral Suppression CHB** |  |  |  |
| HBsAg loss | 1.50% | (0.07-2.2) | (42) |
| To HCC | 0.06% | (0.03-0.09) |  (70% reduction)(31, 32) |
|
| **From Viral Suppression Cirrhosis** |  |  |  |
| HBsAg loss | 1.50% | (0.07-2.2) | (42) |
| To HCC | 0.80% | (0.40-1.20) | (50% reduction) |
| To HBV-related Death | 1.20% | (0.60-1.80) | (50% reduction)  |
| **From Viral Suppression Decompensated Cirrhosis** |  |  |  |
| To HCC | 3% | (1.5-4.5) | (60) |
| To HBV-related Death | 6.10% | (3.05-9.15) | (60) |
| **From Liver Transplantation for Decompensated Cirrhosis** |  |  |  |
| To HBV-related death year 1 | 17%-32% | (8.5-48.0) | (24) |
| To HBV-related death year 2+ | 2.50% | (1.25-24.0) | (24) |
| **From Liver Transplantation for HCC** |  |  |  |
| To HBV-related death year 1 | 16%-39% | (8.0-48.0) | (24) |
| To HBV-related death year 2+ | 2% | (2.0-25.0) | (24) |
| **Gender** |  |  |  |
| Relative Progression Rates for females\* | 0.5 | (0.25-1.0) | (27, 28, 58) |
| Fraction of chronic HBV cases that are Male | 65% | (0.50-0.80) | (2) |

A 50% reduction in disease progression estimates was applied for females

# Appendix Table 5. Incremental Health and Economic Results for a Population of 100,000 adults

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Vaccine and Strategy** | **Cost** | **QALYs** | **ICER** | **Acute Infections** | **Acute Deaths** | **New Chronic Infections** | **Cirrhosis** | **Decompensated Cirrhosis** | **HCC** | **Transplants** | **HBV Deaths** |
| **Heplisav-B**® |  |  |  |  |  |  |  |  |  |  |  |
| Compared to No Vaccination |   |   |   |   |   |   |   |   |   |   |   |
| Status Quo | 5,419,048 | 56 | 96,794 | -1,490 | -2 | -89 | -6 | -1 | -4 | -1 | -6 |
| Compared to Status Quo |   |   |   |   |   |   |   |   |   |   |   |
| HBsAg + Vacc | -40,195,727 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -41,576,587 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -41,626,507 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| **Engerix®/Recombivax ®** |  |  |  |  |  |  |  |  |  |  |  |
| Compared to No Vaccination |   |   |   |   |   |   |   |   |   |   |   |
| Status Quo | 3,464,677 | 51 | 68,225 | -1,338 | -2 | -80 | -5 | -1 | -4 | -1 | -6 |
| Compared to Status Quo |   |   |   |   |   |   |   |   |   |   |   |
| HBsAg + Vacc | -40,190,108 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -41,536,748 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -41,580,815 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| **Twinrix**® |  |  |  |  |  |  |  |  |  |  |  |
| Compared to No Vaccination |   |   |   |   |   |   |   |   |   |   |   |
| Status Quo | 7,175,462 | 51 | 141,297 | -1,338 | -2 | -80 | -5 | -1 | -4 | -1 | -6 |
| Compared to Status Quo |   |   |   |   |   |   |   |   |   |   |   |
| HBsAg + Vacc | -40,324,530 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -42,489,739 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -42,673,809 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |

QALYs: Quality-Adjusted Life-Years

ICER: Incremental Cost-Effectiveness Ratio

HCC: Hepatocellular Carcinoma

HBV: Hepatitis B

# Additional Methodological Detail on probability distributions used for the Monte Carlo simulation:

Each parameter with a range in Table 1, Appendix Table 1, Appendix Table 2, and Appendix Table 3 were described using a probability distribution. The probability distribution had a mean of the base case value and a standard deviation of one quarter of the range. Probabilities and Utilities were parameterized as normal distributions if the range was very narrow as to make the probability of dropping below 0 or going above 1 highly unlikely. Otherwise, they were parameterized as beta distributions. One exception to the probability parameterization was the prevalence. It was parameterized as a gamma distribution, but the standard deviation was 0.0168, so it was unlikely to be greater than 1. Most costs were parameterized as gamma distributions unless the ranges for sensitivity analysis were symmetric. One exception to the rule that the standard deviation was set as one quarter of the range was for the cost of antiviral treatment. For the Monte Carlo simulation, the mean was set at $502, and the standard deviation was set at $173 so as to not have an unduly large standard deviation using the range used for one-way sensitivity analysis. The relative risk of progression for females was also parameterized as a beta distributions. The parameter varying the relative risk of death after liver transplant was parameterized as a normal distribution with a mean of 1 and a standard deviation of 0.25.

# Appendix Table 6a: Detailed Results by age-group (*per-person*): Heplisav vaccination

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Age Group | Strategy | Cost | Eff | Acute Infections | Acute Deaths |  Cirrhosis |  Decompensated Cirrhosis |  HCC |  Transplants |  HBV Deaths |  New Chronic Infections |
|  18-29 | HBsAg, anti-HB s+Vacc | $3,753.96  | 24.80784 | 0.00480 | 0.000006 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00029 |
|   | HBsAg, anti-HBs,anti-HBc+Vacc | $3,754.98  | 24.80784 | 0.00480 | 0.000006 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00029 |
|   | HBsAg +Vacc | $3,772.93  | 24.80784 | 0.00480 | 0.000006 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00029 |
|   | HBsAg only | $3,723.81  | 24.80763 | 0.00949 | 0.000013 | 0.00341 | 0.00088 | 0.00358 | 0.00130 | 0.00555 | 0.00057 |
|   | Status Quo | $4,202.83  | 24.78428 | 0.00480 | 0.000006 | 0.00488 | 0.00137 | 0.00453 | 0.00165 | 0.00729 | 0.00029 |
|   | No Vaccination | $4,150.83  | 24.78407 | 0.00949 | 0.000013 | 0.00490 | 0.00137 | 0.00454 | 0.00165 | 0.00731 | 0.00057 |
| 30-39 | HBsAg, anti-HB s+Vacc | $3,720.55  | 23.61049 | 0.03364 | 0.000045 | 0.00327 | 0.00084 | 0.00342 | 0.00122 | 0.00527 | 0.00202 |
|   | HBsAg, anti-HBs,anti-HBc+Vacc | $3,719.26  | 23.61049 | 0.03364 | 0.000045 | 0.00327 | 0.00084 | 0.00342 | 0.00122 | 0.00527 | 0.00202 |
|   | HBsAg +Vacc | $3,728.27  | 23.61049 | 0.03364 | 0.000045 | 0.00327 | 0.00084 | 0.00342 | 0.00122 | 0.00527 | 0.00202 |
|   | HBsAg only | $3,693.73  | 23.60917 | 0.06650 | 0.000089 | 0.00340 | 0.00086 | 0.00351 | 0.00125 | 0.00542 | 0.00398 |
|   | Status Quo | $4,121.66  | 23.58905 | 0.03364 | 0.000045 | 0.00461 | 0.00131 | 0.00430 | 0.00155 | 0.00687 | 0.00202 |
|   | No Vaccination | $4,084.23  | 23.58773 | 0.06650 | 0.000089 | 0.00474 | 0.00132 | 0.00439 | 0.00158 | 0.00702 | 0.00398 |
| 40-49 | HBsAg, anti-HB s+Vacc | $3,341.94  | 21.41146 | 0.02347 | 0.000032 | 0.00278 | 0.00076 | 0.00298 | 0.00105 | 0.00453 | 0.00141 |
|   | HBsAg, anti-HBs,anti-HBc+Vacc | $3,337.38  | 21.41146 | 0.02347 | 0.000032 | 0.00278 | 0.00076 | 0.00298 | 0.00105 | 0.00453 | 0.00141 |
|   | HBsAg +Vacc | $3,348.05  | 21.41146 | 0.02347 | 0.000032 | 0.00278 | 0.00076 | 0.00298 | 0.00105 | 0.00453 | 0.00141 |
|   | HBsAg only | $3,263.63  | 21.41086 | 0.04638 | 0.000062 | 0.00285 | 0.00077 | 0.00303 | 0.00106 | 0.00460 | 0.00278 |
|   | Status Quo | $3,682.66  | 21.39378 | 0.02347 | 0.000032 | 0.00389 | 0.00117 | 0.00373 | 0.00132 | 0.00587 | 0.00141 |
|   | No Vaccination | $3,595.36  | 21.39318 | 0.04638 | 0.000062 | 0.00396 | 0.00118 | 0.00378 | 0.00133 | 0.00595 | 0.00278 |
| 50-59 | HBsAg, anti-HB s+Vacc | $2,835.02  | 18.15049 | 0.02021 | 0.000027 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00360 | 0.00121 |
|   | HBsAg, anti-HBs,anti-HBc+Vacc | $2,829.84  | 18.15049 | 0.02021 | 0.000027 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00360 | 0.00121 |
|   | HBsAg +Vacc | $2,837.90  | 18.15049 | 0.02021 | 0.000027 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00360 | 0.00121 |
|   | HBsAg only | $2,739.47  | 18.15006 | 0.03996 | 0.000054 | 0.00224 | 0.00066 | 0.00247 | 0.00083 | 0.00366 | 0.00239 |
|   | Status Quo | $3,099.59  | 18.13760 | 0.02021 | 0.000027 | 0.00303 | 0.00100 | 0.00303 | 0.00102 | 0.00463 | 0.00121 |
|   | No Vaccination | $2,998.29  | 18.13718 | 0.03996 | 0.000054 | 0.00307 | 0.00100 | 0.00306 | 0.00103 | 0.00469 | 0.00239 |
| 60+ | HBsAg, anti-HB s+Vacc | $2,405.30  | 15.17054 | 0.01775 | 0.000024 | 0.00171 | 0.00057 | 0.00200 | 0.00064 | 0.00287 | 0.00106 |
|  | HBsAg, anti-HBs,anti-HBc+Vacc | $2,397.56  | 15.17054 | 0.01775 | 0.000024 | 0.00171 | 0.00057 | 0.00200 | 0.00064 | 0.00287 | 0.00106 |
|  | HBsAg +Vacc | $2,404.52  | 15.17054 | 0.01775 | 0.000024 | 0.00171 | 0.00057 | 0.00200 | 0.00064 | 0.00287 | 0.00106 |
|  | HBsAg only | $2,285.00  | 15.17024 | 0.03508 | 0.000047 | 0.00174 | 0.00058 | 0.00202 | 0.00064 | 0.00291 | 0.00210 |
|  | Status Quo | $2,618.73  | 15.16104 | 0.01775 | 0.000024 | 0.00237 | 0.00086 | 0.00248 | 0.00079 | 0.00368 | 0.00106 |
|  | No Vaccination | $2,496.33  | 15.16073 | 0.03508 | 0.000047 | 0.00240 | 0.00086 | 0.00250 | 0.00080 | 0.00372 | 0.00210 |
| Overall | HBsAg, anti-HB s+Vacc | $3,656.42  | 23.80014 | 0.01526 | 0.000021 | 0.00323 | 0.00084 | 0.00341 | 0.00123 | 0.00526 | 0.00091 |
|  | HBsAg, anti-HBs,anti-HBc+Vacc | $3,655.92  | 23.80014 | 0.01526 | 0.000021 | 0.00323 | 0.00084 | 0.00341 | 0.00123 | 0.00526 | 0.00091 |
|  | HBsAg +Vacc | $3,670.23  | 23.80014 | 0.01526 | 0.000021 | 0.00323 | 0.00084 | 0.00341 | 0.00123 | 0.00526 | 0.00091 |
|  | HBsAg only | $3,618.92  | 23.79958 | 0.03016 | 0.000041 | 0.00329 | 0.00085 | 0.00345 | 0.00124 | 0.00532 | 0.00181 |
|  | Status Quo | $4,072.18  | 23.77829 | 0.01526 | 0.000021 | 0.00461 | 0.00131 | 0.00431 | 0.00156 | 0.00690 | 0.00091 |
|  | No Vaccination | $4,017.99  | 23.77773 | 0.03016 | 0.000041 | 0.00467 | 0.00132 | 0.00435 | 0.00157 | 0.00696 | 0.00181 |

# Appendix Table 6b: Detailed Results by age-group: Engerix/Recombivax HB

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age Group** | **Strategy** | **Cost** | **Eff** | **Acute Infections** | **Acute Deaths** |  **Cirrhosis** |  **Decompensated Cirrhosis** |  **HCC** |  **Transplants** |  **HBV Deaths** |  **New Chronic Infections** |
| 18-29 | HBsAg, anti-HBs + Vacc | $3,739.04  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,740.06  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg + Vacc | $3,757.61  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg only | $3,723.81  | 24.80763 | 0.00949 | 0.000013 | 0.00341 | 0.00088 | 0.00358 | 0.00130 | 0.00555 | 0.00057 |
|  | Status Quo | $4,187.44  | 24.78427 | 0.00515 | 0.000007 | 0.00488 | 0.00137 | 0.00453 | 0.00165 | 0.00729 | 0.00031 |
|  | No Vaccination | $4,150.83  | 24.78407 | 0.00949 | 0.000013 | 0.00490 | 0.00137 | 0.00454 | 0.00165 | 0.00731 | 0.00057 |
| 30-39 | HBsAg, anti-HBs + Vacc | $3,695.69  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,694.51  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg + Vacc | $3,703.15  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg only | $3,693.73  | 23.60917 | 0.06650 | 0.000089 | 0.00340 | 0.00086 | 0.00351 | 0.00125 | 0.00542 | 0.00398 |
|  | Status Quo | $4,096.48  | 23.58895 | 0.03610 | 0.000049 | 0.00462 | 0.00131 | 0.00431 | 0.00155 | 0.00688 | 0.00216 |
|  | No Vaccination | $4,084.23  | 23.58773 | 0.06650 | 0.000089 | 0.00474 | 0.00132 | 0.00439 | 0.00158 | 0.00702 | 0.00398 |
| 40-49 | HBsAg, anti-HBs + Vacc | $3,317.82  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,313.43  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg + Vacc | $3,323.68  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg only | $3,263.63  | 21.41086 | 0.04638 | 0.000062 | 0.00285 | 0.00077 | 0.00303 | 0.00106 | 0.00460 | 0.00278 |
|  | Status Quo | $3,658.23  | 21.39367 | 0.02794 | 0.000038 | 0.00391 | 0.00117 | 0.00374 | 0.00132 | 0.00589 | 0.00167 |
|  | No Vaccination | $3,595.36  | 21.39318 | 0.04638 | 0.000062 | 0.00396 | 0.00118 | 0.00378 | 0.00133 | 0.00595 | 0.00278 |
| 50-59 | HBsAg, anti-HBs + Vacc | $2,807.92  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $2,802.94  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg + Vacc | $2,810.61  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg only | $2,739.47  | 18.15006 | 0.03996 | 0.000054 | 0.00224 | 0.00066 | 0.00247 | 0.00083 | 0.00366 | 0.00239 |
|  | Status Quo | $3,072.25  | 18.13752 | 0.02407 | 0.000032 | 0.00304 | 0.00100 | 0.00304 | 0.00102 | 0.00464 | 0.00144 |
|  | No Vaccination | $2,998.29  | 18.13718 | 0.03996 | 0.000054 | 0.00307 | 0.00100 | 0.00306 | 0.00103 | 0.00469 | 0.00239 |
| 60+ | HBsAg, anti-HBs + Vacc | $2,376.62  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $2,369.14  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg + Vacc | $2,375.70  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg only | $2,285.00  | 15.17024 | 0.03508 | 0.000047 | 0.00174 | 0.00058 | 0.00202 | 0.00064 | 0.00291 | 0.00210 |
|  | Status Quo | $2,589.85  | 15.16095 | 0.02292 | 0.000031 | 0.00238 | 0.00086 | 0.00248 | 0.00079 | 0.00369 | 0.00137 |
|  | No Vaccination | $2,496.33  | 15.16073 | 0.03508 | 0.000047 | 0.00240 | 0.00086 | 0.00250 | 0.00080 | 0.00372 | 0.00210 |
| Overall | HBsAg, anti-HBs + Vacc | $3,637.27  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,636.83  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg + Vacc | $3,650.74  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg only | $3,618.92  | 23.79958 | 0.03016 | 0.000041 | 0.00329 | 0.00085 | 0.00345 | 0.00124 | 0.00532 | 0.00181 |
|  | Status Quo | $4,052.64  | 23.77824 | 0.01678 | 0.000023 | 0.00462 | 0.00131 | 0.00431 | 0.00156 | 0.00690 | 0.00101 |
|  | No Vaccination | $4,017.99  | 23.77773 | 0.03016 | 0.000041 | 0.00467 | 0.00132 | 0.00435 | 0.00157 | 0.00696 | 0.00181 |

# Appendix Table 6c: Detailed Results by age-group: Twinrix

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age Group** | **Strategy** | **Cost** | **Eff** | **Acute Infections** | **Acute Deaths** |  **Cirrhosis** |  **Decompensated Cirrhosis** |  **HCC** |  **Transplants** |  **HBV Deaths** |  **New Chronic Infections** |
| 18-29 | HBsAg, anti-HBs + Vacc | $3,754.08  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,755.01  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg + Vacc | $3,782.32  | 24.80782 | 0.00515 | 0.000007 | 0.00339 | 0.00087 | 0.00357 | 0.00129 | 0.00553 | 0.00031 |
|  | HBsAg only | $3,723.81  | 24.80763 | 0.00949 | 0.000013 | 0.00341 | 0.00088 | 0.00358 | 0.00130 | 0.00555 | 0.00057 |
|  | Status Quo | $4,213.50  | 24.78427 | 0.00515 | 0.000007 | 0.00488 | 0.00137 | 0.00453 | 0.00165 | 0.00729 | 0.00031 |
|  | No Vaccination | $4,150.83  | 24.78407 | 0.00949 | 0.000013 | 0.00490 | 0.00137 | 0.00454 | 0.00165 | 0.00731 | 0.00057 |
| 30-39 | HBsAg, anti-HBs + Vacc | $3,738.62  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,734.92  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg + Vacc | $3,752.54  | 23.61039 | 0.03610 | 0.000049 | 0.00328 | 0.00085 | 0.00343 | 0.00123 | 0.00528 | 0.00216 |
|  | HBsAg only | $3,693.73  | 23.60917 | 0.06650 | 0.000089 | 0.00340 | 0.00086 | 0.00351 | 0.00125 | 0.00542 | 0.00398 |
|  | Status Quo | $4,147.21  | 23.58895 | 0.03610 | 0.000049 | 0.00462 | 0.00131 | 0.00431 | 0.00155 | 0.00688 | 0.00216 |
|  | No Vaccination | $4,084.23  | 23.58773 | 0.06650 | 0.000089 | 0.00474 | 0.00132 | 0.00439 | 0.00158 | 0.00702 | 0.00398 |
| 40-49 | HBsAg, anti-HBs + Vacc | $3,364.78  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,356.15  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg + Vacc | $3,376.64  | 21.41135 | 0.02794 | 0.000038 | 0.00280 | 0.00076 | 0.00299 | 0.00105 | 0.00454 | 0.00167 |
|  | HBsAg only | $3,263.63  | 21.41086 | 0.04638 | 0.000062 | 0.00285 | 0.00077 | 0.00303 | 0.00106 | 0.00460 | 0.00278 |
|  | Status Quo | $3,712.54  | 21.39367 | 0.02794 | 0.000038 | 0.00391 | 0.00117 | 0.00374 | 0.00132 | 0.00589 | 0.00167 |
|  | No Vaccination | $3,595.36  | 21.39318 | 0.04638 | 0.000062 | 0.00396 | 0.00118 | 0.00378 | 0.00133 | 0.00595 | 0.00278 |
| 50-59 | HBsAg, anti-HBs + Vacc | $2,857.61  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $2,847.99  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg + Vacc | $2,864.95  | 18.15041 | 0.02407 | 0.000032 | 0.00220 | 0.00066 | 0.00244 | 0.00082 | 0.00362 | 0.00144 |
|  | HBsAg only | $2,739.47  | 18.15006 | 0.03996 | 0.000054 | 0.00224 | 0.00066 | 0.00247 | 0.00083 | 0.00366 | 0.00239 |
|  | Status Quo | $3,127.94  | 18.13752 | 0.02407 | 0.000032 | 0.00304 | 0.00100 | 0.00304 | 0.00102 | 0.00464 | 0.00144 |
|  | No Vaccination | $2,998.29  | 18.13718 | 0.03996 | 0.000054 | 0.00307 | 0.00100 | 0.00306 | 0.00103 | 0.00469 | 0.00239 |
| 60+ | HBsAg, anti-HBs + Vacc | $2,432.72  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $2,419.06  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg + Vacc | $2,435.24  | 15.17045 | 0.02292 | 0.000031 | 0.00172 | 0.00058 | 0.00200 | 0.00064 | 0.00288 | 0.00137 |
|  | HBsAg only | $2,285.00  | 15.17024 | 0.03508 | 0.000047 | 0.00174 | 0.00058 | 0.00202 | 0.00064 | 0.00291 | 0.00210 |
|  | Status Quo | $2,650.74  | 15.16095 | 0.02292 | 0.000031 | 0.00238 | 0.00086 | 0.00248 | 0.00079 | 0.00369 | 0.00137 |
|  | No Vaccination | $2,496.33  | 15.16073 | 0.03508 | 0.000047 | 0.00240 | 0.00086 | 0.00250 | 0.00080 | 0.00372 | 0.00210 |
| Overall | HBsAg, anti-HBs + Vacc | $3,664.85  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg, anti-HBs, anti-HBc + Vacc | $3,663.01  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg + Vacc | $3,686.50  | 23.80009 | 0.01678 | 0.000023 | 0.00324 | 0.00084 | 0.00341 | 0.00123 | 0.00527 | 0.00101 |
|  | HBsAg only | $3,618.92  | 23.79958 | 0.03016 | 0.000041 | 0.00329 | 0.00085 | 0.00345 | 0.00124 | 0.00532 | 0.00181 |
|  | Status Quo | $4,089.75  | 23.77824 | 0.01678 | 0.000023 | 0.00462 | 0.00131 | 0.00431 | 0.00156 | 0.00690 | 0.00101 |
|  | No Vaccination | $4,017.99  | 23.77773 | 0.03016 | 0.000041 | 0.00467 | 0.00132 | 0.00435 | 0.00157 | 0.00696 | 0.00181 |

# Evaluation of Vaccination interventions in comparison to interventions without vaccination

Interventions that included vaccination increased costs slightly, but also increased QALYs. The lowest overall cost strategy was one that includes HBsAg testing and treatment without vaccination. When compared to HBsAg testing and treatment without vaccination, vaccination added health benefits, but at increased costs (Appendix Tables 4a, b, and c). Because all the vaccination strategies differed only in the number of immune people they avoided vaccinating, the health benefits added by vaccination were similar in the three strategies: HBsAg screening and vaccination; HBsAg, Anti-HBs screening and vaccination; and HBsAg, Anti-HBs, Anti-HBc screening and vaccination. Per 100,000 people at an STI clinic, between 1338 and 1490 acute infections are averted, 6 HBV-related deaths are averted, and 51-56 QALYs are gained (Table 2, Appendix Tables 4a, b, and c, and Appendix Table 5). These results are somewhat modest because most of the cohort already has immunity from prior vaccination or natural infection. 58% of the population is under the age of 30 and 91% of those younger individuals have already been vaccinated. Overall, about 25% could benefit from vaccination, and not all of them will actually receive a vaccine or all the doses. Of those unprotected, about 29% are age 40 and older and face a lower incidence of acute infection, and 53% are in their 30’s and will also soon face a lower incidence of acute infection.

Vaccination for this population can be expensive. Without any testing, vaccination adds $ 3.46 million (Engerix-B®/Recombivax HB®), $5.42 million (Heplisav®), or 7.18 milllion (Twinrix®) for a cohort of 100,000. However, HBsAg testing identifies individuals in need of treatment and Anti-HBs and Anti-HBc testing helps focus vaccine doses on those who may benefit from vaccination. Again, the different vaccination strategies that included HBsAg testing and treatment all had the same health outcomes since adding core or surface antibody tests did not change the number of people treated or susceptible people vaccinated. However, adding core or surface antibody tests did identify people who might not benefit from vaccination, so second or third doses of vaccine could be avoided, and costs saved. Screening strategies of “HBsAg, anti-HBc, anti-HBs and vaccination” and “HBsAg, anti-HBs, and vaccination” had very similar costs adding above HBsAg testing without vaccination in a cohort of 100,000. They added 51 (Engerix-B®/Recombivax HB®, Twinrix®) or 56 (Heplisav®) additional QALYs, for an ICER of $35,279-36,147 (Engerix-B®/Recombivax HB®), $86,828-90,453 (Twinrix®) or $66,093-66,985 (Heplisav®) per QALY when compared to HBsAg testing without vaccination (Appendix Tables 4a-c).

Although they involved higher costs of tests, these screening strategies involving Anti-HBs tests were lower-cost than “HBsAg and vaccination” because the increased test costs were outweighed by the costs of unnecessary vaccine doses avoided.

# Sensitivity Analysis Impact of Value of Screening and Vaccination vs. Status Quo

# Appendix Figure 3a: Net Monetary Value Increase with 3 tests and Vaccination vs. Status Quo for a single person screened. Heplisav® vaccine.

# Appendix Figure 3b: Net Monetary Value Increase with 3 tests and Vaccination vs. Status Quo for a single person screened. Engerix-B®/Recombivax HB® vaccine.

Net Monetary value calculates the incremental value of the HBsAg, anti-HBs, anti-HBc + Vacc strategy compared to the status quo strategy by valuing dollars at a rate of $1 = $1 and QALYs gained at a value of 1 QALY = $100,000. Positive values indicate the HBsAg, anti-HBs, anti-HBc + Vacc strategy is preferred when compared to the status quo if a policymaker is willing to pay $100,000 per QALY gained.

# Appendix Figure 3c: Net Monetary Value Increase with 3 tests and Vaccination vs. Status Quo for a single person screened. Twinrix® vaccine.

Net Monetary value calculates the incremental value of the HBsAg, anti-HBs, anti-HBc + Vacc strategy compared to the status quo strategy by valuing dollars at a rate of $1 = $1 and QALYs gained at a value of 1 QALY = $100,000. Positive values indicate the HBsAg, anti-HBs, anti-HBc + Vacc strategy is preferred when compared to the status quo if a policymaker is willing to pay $100,000 per QALY gained.

# Appendix Figure 4a: Sensitivity Analysis on Prevalence of HBsAg on Cost-Savings of Screening With Three Tests Versus the Status Quo (Heplisav®)

# Appendix Figure 4b: Sensitivity Analysis on Prevalence of HBsAg on Cost-Savings of Screening With Three Tests Versus the Status Quo (Engerix®)

# Appendix Figure 4c: Sensitivity Analysis on Prevalence of HBsAg on Cost-Savings of Screening With Three Tests Versus the Status Quo (Twinrix®)

# Appendix Figure 5a: Sensitivity Analysis on Prevalence of Anti-HBc on Cost-Savings of Screening With Three Tests Versus the Status Quo (Heplisav®)

# Appendix Figure 5b: Sensitivity Analysis on Prevalence of Anti-HBc on Cost-Savings of Screening With Three Tests Versus the Status Quo (Engerix®)

# Appendix Figure 5c: Sensitivity Analysis on Prevalence of Anti-HBc on Cost-Savings of Screening With Three Tests Versus the Status Quo (Twinrix®)

# Sensitivity Analysis on the relative economic value of screening with three tests vs. two tests:

# Figure 6a, Heplisav®

# Figure 6b, Engerix-B®/Recombivax HB®

# Figure 6c, Twinrix ®

# Evaluation of lower-cost vaccination:

Using CDC negotiated pricing instead of private payer pricing makes immunization much more cost-effective. The ICER of the Status Quo compared to no vaccination becomes much more favorable at $44,374 per QALY for Heplisav®, $16,298 for Engerix-B®/Recombivax HB®), and $68,944 for Twinrix® (Appendix Tables 7a-c).

# Appendix Table 7a: Incremental Health and Economic Results for a Population of 100,000 adults: CDC Negotiated Pricing (Heplisav-B®)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Strategy** | **Cost** | **QALYs** | **ICER** | **Acute Infections** | **Acute Deaths** | **New Chronic Infections** | **Cirrhosis** | **Decompensated Cirrhosis** | **HCC** | **Transplants** | **HBV Deaths** |

|  |
| --- |
| **Compared to No Vaccination** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Status Quo | 2,484,280 | 56 | 44,374 | -1,490 | -2 | -89 | -6 | -1 | -4 | -1 | -6 |

|  |
| --- |
| **Screening Compared to Status Quo** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| HBsAg + Vacc | -40,112,331 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -40,985,345 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -40,948,405 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |

# Table 7b: Incremental Health and Economic Results for a Population of 100,000 adults: CDC Negotiated Pricing (Engerix-B®/Recombivax HB®)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Strategy** | **Cost** | **QALYs** | **ICER** | **Acute Infections** | **Acute Deaths** | **New Chronic Infections** | **Cirrhosis** | **Decompensated Cirrhosis** | **HCC** | **Transplants** | **HBV Deaths** |

|  |
| --- |
| **Compared to No Vaccination** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Status Quo | 827,679 | 51 | 16,298 | -1,338 | -2 | -80 | -5 | -1 | -4 | -1 | -6 |

|  |
| --- |
| **Screening Compared to Status Quo** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| HBsAg + Vacc | -40,094,583 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -40,859,524 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -40,804,100 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |

# Table 7c: Incremental Health and Economic Results for a Population of 100,000 adults: CDC Negotiated Pricing (Twinrix®)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Strategy** | **Cost** | **QALYs** | **ICER** | **Acute Infections** | **Acute Deaths** | **New Chronic Infections** | **Cirrhosis** | **Decompensated Cirrhosis** | **HCC** | **Transplants** | **HBV Deaths** |

|  |
| --- |
| **Compared to No Vaccination** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Status Quo | 3,501,191 | 51 | 68,944 | -1,338 | -2 | -80 | -5 | -1 | -4 | -1 | -6 |

|  |
| --- |
| **Screening Compared to Status Quo** |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| HBsAg + Vacc | -40,191,431 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs + Vacc | -41,546,125 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |
| HBsAg, anti-HBs, anti-HBc + Vacc | -41,591,570 | 2,185 |   | 0 | 0 | 0 | -138 | -47 | -90 | -33 | -163 |

QALYs: Quality-Adjusted Life-Years

ICER: Incremental Cost-Effectiveness Ratio

Dominant: the intervention has lower costs and higher QALYs than the Status Quo

**Sensitivity Analysis Impact on value of vaccination compared to no vaccination**

The main manuscript presents some cost-effectiveness results comparing the status quo (with no screening) compared to a no vaccination strategy. However, because the status quo does not include screening, it also includes many costly, unnecessary vaccine doses.

Here, in the appendix, we compare “screening and vaccination” strategies to “screening and no vaccination” strategies. In this section, the ICERs look better because adding screening to vaccination avoids those unnecessary, costly vaccine doses.

When compared to HBsAg screening and treatment alone without vaccination, the value of screening with three tests, treating, and vaccinating had an ICER of $77,747 (Heplisav®), $46,818 Engerix-B®/Recombivax HB®), or $98,367 (Twinrix®) per QALY gained. These ICER values are slightly better than the ICERs of the status quo compared to no vaccination because these strategies involved screening, which avoided some of the costs of unnecessary vaccine doses.

The value of vaccination was sensitive to parameter assumptions (Appendix Figures 7a-c). The most sensitive parameter was the probability that an acute infection would become a chronic, lifelong infection. At a low value of only a 3% chance, the incremental cost-effectiveness ratio was ICER of $141,000, (Heplisav®), $98,000 Engerix-B®/Recombivax HB®), or $170,000 (Twinrix®) per QALY gained. Other parameters related to the costs of acute infection, like the probability acute infections led to hospitalization, fulminant hepatitis, chronic infection, or death were also important to the cost-effectiveness of vaccination. Some parameter values could make vaccination cost-saving.

The ICER of testing and vaccination can look better (or worse) if the vaccination strategy is applied to a population age group that could receive more (or less) benefit. For those in their 20’s vaccination may not have been as cost-effective because prevalence of prior vaccination was already quite high. Screening and vaccinating with Engerix-B®/Recombivax HB® could be cost-saving for those in their early 30’s as this population was old enough to not be likely to have been vaccinated, but young enough to still have risks of HBV infection and still have a risk of an acute infection becoming chronic and leading to complications later in life. However, for those in their late 40’s and above, the ICERs rose very high because of the limited remaining lifetime of HBV infection risk and benefit of vaccination. (Appendix Figures 8a-c)

If incidence decreases substantially, the ICER of vaccination strategies increases. Similarly, if incidence increases substantially, the ICER of vaccination strategies reduces. (Appendix Figures 9a-c). With 50% higher incidence, vaccination with Heplisav® and Twinrix® can have ICERs below $50,000 per QALY.

The way the model is constructed, if prevalence of HBsAg decreases, more individuals are susceptible to HBV infection. So, as prevalence of HBsAg decreases, more individuals are susceptible to HBV infection, and thus may benefit from HBV immunization (Appendix Figures 10a-c). ).

If awareness of prior HBV immunization is close to 100%, then the ICER of vaccination drops substantially because there is a much lower risk of unnecessary vaccination (Appendix Figures 11a-c). Vaccination with Heplisav® can have ICERs below $50,000 per QALY.

Probabilistic sensitivity analysis highlights the uncertainty in which specific testing and vaccination strategy is the optimal one (Appendix Figures 12a-c), and in particular, when comparing against all strategies, including a strategy of HBsAg testing and treatment without vaccination.

# Appendix Figure 7a: Tornado Diagram of Vaccination Versus No Vaccination (Heplisav ®)

# Figure 7b, Engerix-B®/Recombivax HB®

# Figure 7c, Twinrix®

ICER: Incremental Cost-Effectiveness Ratio

“3 test and vaccination” is HBsAg, anti-HBs, anti-HBc and Vaccination

# Appendix Figure 8a: Results by Age: Incremental Cost-Effectiveness Ratio of Testing with HBsAg, anti-HBs, anti-HBc + Vacc vs. HBsAg testing without Vaccination Heplisav®

# Appendix Figure 8b: Engerix-B®/Recombivax HB®

# Appendix Figure 8c: Twinrix®

ICER: Incremental Cost-Effectiveness Ratio

# Appendix Figure 9a: Sensitivity to Incidence including strategies with no vaccination. HBsAg, anti-HBs, anti-HBc + Vacc vs HBsAg testing only, no Vaccination (Heplisav®)

# Appendix Figure 9b: HBsAg, anti-HBs, anti-HBc + Vacc vs HBsAg testing only, no Vaccination: Engerix-B®/Recombivax HB®

# Appendix Figure 9c: HBsAg, anti-HBs, anti-HBc + Vacc vs HBsAg testing only, no Vaccination: Twinrix®

ICER: Incremental Cost-Effectiveness Ratio

# Appendix Figure 10a: Sensitivity to the Prevalence of HBsAg comparing to no vaccination (Heplisav®)

# Appendix Figure 10b: Engerix-B®/Recombivax HB®

# Appendix Figure 10c: Twinrix®

Note: As prevalence of HBsAg declines, there are more unprotected individuals.

# Appendix Figure 11a. Sensitivity to awareness of prior vaccination comparing to no vaccination (Heplisav®)

# Appendix Figure 11b: Engerix-B®/Recombivax HB®

# Appendix Figure 11c: Twinrix®

# Appendix Figure 12a: Cost-Effectiveness Acceptability Curves NOT including strategies with no vaccination. (Engerix®/Recombivax®)

# Appendix Figure 12b: Cost-Effectiveness Acceptability Curves NOT including strategies with no vaccination. (Twinrix®)

# Appendix Figure 13a: Cost-Effectiveness Acceptability Curves including strategies with no vaccination. (Heplisav®)

# Appendix Figure 13b: Engerix-B®/Recombivax HB®

# Appendix Figure 13c: Twinrix®

QALY: Quality-Adjusted Life Year