Selective hepatitis B birth dose vaccination in São Tomé and Príncipe: a program assessment and cost-effectiveness study

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Abstract

Background: São Tomé and Príncipe (STP), a country that is highly endemic for hepatitis B (HBV), currently uses a selective HBV birth-dose vaccination (HepB-BD) strategy targeting infants born to mothers who screen positive for HBV surface antigen (HBsAg) during routine prenatal visits. We conducted a field assessment and economic analysis of the HepB-BD program to provide evidence to guide development of cost-effective policies to prevent perinatal HBV transmission in STP.

Methods: We interviewed national stakeholders and key informants, as well as supervisors and healthcare workers from all five healthcare facilities (HCF) that provide maternity services on the island of São Tomé, to understand policies, norms, knowledge, and practices related to HepB-BD, vaccine management, and data recording/reporting. Cost-effectiveness of the existing program compared to an alternate approach of universal HepB-BD administration to all newborns was calculated using a decision analytic model and expressed as an incremental cost effectiveness ratios (ICERs), in 2015 US$ per HBV-associated death and per chronic HBV case prevented, from the STP healthcare system perspective.

Results: We found that STP lacked national or facility-specific written policies and procedures related to HepB-BD; however, knowledge regarding HepB-BD was high, and practices were generally uniform between facilities. Though timeliness of HepB-BD is not documented or monitored, immediate administration of HepB-BD to eligible newborns was considered a high priority by all informants. Compared to the existing selective vaccination strategy, universal HepB-BD would result in a 19% decrease in chronic HBV infection per year at an overall cost savings of approximately 44%. We estimate a cost-effectiveness ratio of US$5,012 saved per HBV-associated death averted.

Conclusions: The existing selective HepB-BD program in STP is of high quality and well-implemented, but can be improved and made more effective and save costs by adopting a universal newborn HBV-BD program without maternal HBsAg screening.

Background

It is estimated that 85-90% of hepatitis B virus (HBV)-associated deaths are vaccine preventable [1]. Worldwide, 30% of cirrhosis and 53% of hepatocellular cancer deaths are attributable to chronic HBV infection [2]. The most important risk factor for chronic HBV infection is acquisition early in life, especially perinatal infection, which has approximately 70—90% risk of chronic persistence [3–5]. The World Health Organization (WHO) recommends administration of a birth-dose of HBV vaccine (HepB-BD) to all newborns, preferably within 24 hours of delivery, which is 80-90% effective in preventing HBV transmission during childbirth [5].

São Tomé and Príncipe (STP), with population of approximately 193,000 and annual birth cohort of approximately 6400 [6], is considered highly endemic for chronic HBV, with seroprevalence of 10% in men and 6.1% in women [7]. STP introduced a program in 2002 to administer HepB-BD to infants born to HBV-infected women identified by screening during routine prenatal visits. Because only selected infants are targeted for vaccination, national coverage of HepB-BD is low (3%)[8]; however, STP has high coverage of pre-natal services (97.5% with at least 1 ANC visit) and attended births at a healthcare facility (91%) [9]. Coverage of HepB-BD among infants born to HBV-seropositive women is correspondingly high (national estimate 92%). All mothers are strongly encouraged to deliver in a district hospital, and the program lacks the capacity to support home births.

We conducted an assessment of the HepB-BD program in STP to characterize and document the national policies related to HepB-BD, policy implementation and practices in national and district hospitals, barriers to complete coverage of HepB-BD among all infants born to HBV-seropositive women, reporting practices related to HepB-BD, and knowledge and attitudes of healthcare providers. Additionally, this study aimed to evaluate the cost-effectiveness of the existing selective HepB-BD program as compared to a WHO-recommended universal HepB-BD program in order to provide evidence-based recommendations to the country to guide any future policy change.

Methods

Hepatitis B birth dose vaccination program assessment

During August 2015, we assessed facilities that provide maternity services in STP. The evaluation was planned to be conducted in six health facilities: five facilities on Sao Tome island that provide maternity services – the national referral hospital, three district public hospitals, and one health post – and one district public hospital on the island of Principe, which could not be reached due to transportation difficulties. In addition, we collected information from key informants in the Ministry of Health (MOH), and representatives from partners and stakeholder organizations regarding the policies, practices, and barriers related to HepB-BD implementation.

Structured and unstructured survey questions were developed during a consultative workshop at the World Health Organization Regional Office for Africa (WHO-AFRO) headquarters. MOH officers were interviewed regarding HepB-BD policy, training, supervision, vaccine management, and coverage monitoring. At each facility, key Expanded Programme on Immunization (EPI) and/or maternity staff were interviewed on birth dose policy, practice, and knowledge, including policies and practices related to home births. Newborn log books and monthly monitoring reports were reviewed to evaluate the number of newborns who received HepB-BD and the timing of the dose.

Study data were collected and managed using REDCap electronic data capture tools (Vanderbilt University, Nashville, TN) [10]. Simple descriptive analyses using R (R Foundation for Statistical Computing, Vienna, Austria) [11] were performed to summarize the findings using one-way frequencies.

Cost-effectiveness analysis

We conducted a cost-effectiveness analysis to guide the STP MOH in formulating policy to reduce HBV-related health burden using HepB-BD. We created a decision analytic model (Appendix A) using @RISK (Palisade Software, Ithaca, New York) to compare the current policy in STP ("base case") against a hypothetical alternative policy ("alternative") of universal facility-based vaccination of all newborn infants without maternal HBsAg screening.

Selective and universal vaccination policy assumptions

Under the base case policy, pregnant women undergo screening for HBsAg using a rapid test (ALERE, Waltham, Massachusetts) [12] as part of routine preventive antenatal care. Following delivery in a healthcare facility (HCF), infants born to women known to be HBsAg-positive are administered HBV-BD. Women whose HBsAg status is unknown are tested if they present to a HCF in labor. Under the hypothetical alternative policy of universal facility-based birth dose vaccination, routine prenatal HBsAg testing would be discontinued and all infants would be vaccinated within 24 hours of delivery. We assumed that there would continue to be no outreach program to provide HepB-BD outside of a HCF.

Decision analytic model assumptions and data sources

A Markov transitional probability model was used to follow a hypothetical annual pregnancy cohort of 6487 mothers [6][13] and their newborns during their lifetime to determine the costs and effects of providing the two vaccination programs to this pregnancy cohort and newborns. The primary cost-effectiveness measure evaluated was the incremental cost-effectiveness ratio (ICER), interpreted as US$ per death averted by HBV birth-dose vaccination. Other effects include the total number of chronic HBV infections, total number of HBV-related deaths, and ICER expressed as unit cost per chronic HBV infection averted. We did not consider any secondary benefits of vaccination, and only infections due to vertical transmission were considered in this model.

The decision analytic model included the following states of health that could be experienced during the lifetime of a birth cohort member: infected or uninfected with HBV, progression to chronic HBV, death due to hepatitis B complications, or death unrelated to hepatitis B. Transition probabilities, vaccine effectiveness, epidemiological data, and cost assumptions were sourced from published literature data whenever available (Table 2) [3,7,9,13–23]. We assumed maternal HBV prevalence of 6.1% based on recent serological survey data [7]. We accounted for the differential vertical transmission risk associated with the hepatitis B e antigen (HBeAg) status of the mother [17,24,25]. Although high-quality STP-specific age- and gender-specific serological data exist on the prevalence of hepatitis B infection, no data exist on HBeAg prevalence in STP. We therefore assumed that 30.6% of HBsAg positive mothers were HBeAg positive, based on published 2005 estimates for HBeAg prevalence in West sub-Saharan Africa among women aged 20-29 [23]. Estimates for the 10-19 year and 40-49 year age range were used as upper and lower bounds, respectively [23]. For HepB-BD coverage in hospitals, we used the national estimate for percent coverage of birth-dose among HBV positive mothers.

Cost assumptions and data sources

The cost-effectiveness analysis was conducted from the STP healthcare system perspective inclusive of all payers, with a lifetime analytic horizon and a 12-month time-frame for costs, which are expressed in

2015 US dollars (US$). Societal indirect costs due to lost productivity from hepatitis B morbidity and mortality are therefore not included. We chose an incremental approach to assess costs in this study, and therefore only included costs that would be directly attributable to the startup costs, increased personnel demand and materials specifically associated with the implementation of an alternative HepB-BD program [26,27]. We assumed that startup costs associated with initial introduction of the existing HepB-BD program, and shared overhead costs such as hospital electricity and support staff, and immunization progam manager time, were absorbed by the health system. Direct non-medical costs borne by parents (e.g., transportation to healthcare facilities) and indirect costs (e.g., productivity losses due to time spent obtaining healthcare services) related to HBsAg screening or vaccination are not included, as both interventions would occur as part of routine antenatal and postpartum care under either scenario. No costs of treatment of HBV complications were included, as specific treatments for these complications are not routinely available in STP.

For vaccination costs, under the base case of selective vaccination, we included the unit cost of the vaccine [28], as well as costs of cold-chain maintenance, program management, record keeping, routine facility-based service delivery, supervision, and surveillance drawn from a recent cost study of pneumococcus vaccination in Benin [20]. Costs of screening included the unit cost of the maternal screening test (Communication with Luis Manuel do Sacramento Bonfim, Health Specialist, UNICEF STP), and personnel time associated with rapid test performance, and pre-and post-test counseling. We assumed post-test counseling in the case of negative tests would be negligible. Personnel costs were extrapolated using the estimated personnel time burden rapid syphilis testing in routine antenatal care in Haiti, [21] and nursing salary costs from Comoros and Cote d'Ivoire, West African nations with similar GDP [22].

For universal vaccination, additional incremental costs associated with training, advocacy and social mobilization associated with the change in the program from selective to universal vaccination were included, also sourced from the Benin pneumococcus vaccine cost study [20]. We assumed that vaccine transportation and storage capacity in the MNCH/EPI system were not at maximum and that no additional specific personnel or capital equipment costs were associated with HBV monovalent vaccine in either the base-case or the increased number of doses required for universal vaccination. We assumed that under a universal vaccination program, hepatitis B rapid testing would not be continued as part of routine antenatal care (ANC), and therefore did not include those costs.

Model uncertainty and sensitivity analyses

Uncertainty was incorporated into the estimates by modeling inputs as β-PERT distribution [CITE – ask Sarah] using the base-case and ranges listed in Table 1 for alpha and beta parameters. A total of 10,000 simulations were performed, using random draws from the probability distributions as inputs to the model. The 50, 2.5 and 97.5 percentiles of the Monte Carlo simulation results were used to report the estimate and 95% confidence interval (95% CI) for infections, chronic cases, HBV-associated deaths, and ICERs. In addition, one-way sensitivity analyses were conducted to estimate the impact of variations to key assumptions that were not directly sourced from published data. We varied the assumed birth-dose coverage for hospital births and home births, the proportion of mothers tested for HBV during ANC, proportion without ANC care who deliver in a facility, and the rate of hospital-based HBV rapid testing of women who did not receive ANC. We varied the supply unit price and service delivery costs of both vaccination and HBsAg rapid testing from 0% to 200%.

Results

Hepatitis B birth dose program assessment

All facilities that offered maternity services reported providing HepB-BD according to the national selective vaccination policy. Findings of the HepB-BD programmatic assessment are summarized in Table 1. Despite the absence of specific written policies and procedures related to HepB-BD, knowledge regarding HepB-BD was high, and practices were generally uniform. We identified one important knowledge gap regarding false contraindications to HepB-BD: HCF staff universally believed that breastfeeding should be withheld until after HepB-BD administration in order to prevent vertical HBV transmission, which is contrary to WHO recommendations [1,5].

We identified very few barriers to HepB-BD administration to infants of HBsAg-positive mothers. Mothers who did not attend ANC, or whose ANC records (either home-based record or clinic-based records) could not be located, were reportedly tested for HBsAg during delivery if they presented for a facility birth in order to determine if the infant should receive HepB-BD vaccination. Mothers who were HBsAg positive reportedly receive extra counseling on the importance of seeking facility births or, in the case of an unplanned home birth, bringing their infant for postnatal care immediately in order to ensure the infant receives HepB-BD.

During our assessment, coverage of HepB-BD among infants of HBsAg-positive mothers could not be independently calculated, as HBsAg status of mothers admitted to maternity wards was not documented unless the infant was vaccinated. Date of HepB-BD administration was not recorded by any of the sampled facilities, and timeliness of HBV-BD administration could not be assessed.

Cost-effectiveness of selective vs. universal HepB-BD vaccination

We found that implementation of a universal HepB-BD program would result in a 19% decrease in chronic HBV infection per year, and would prevent one additional death HBV related death per annual birth cohort, compared to the current selective vaccination base-case strategy (Table 2). Furthermore, a universal HepB-BD program would result in an overall cost savings to the STP healthcare system of approximately 44%.

The confidence intervals in the estimates reflect the deterministic uncertainty in the model resulting from the ranges of available data used to build the model. Figure 1 shows the relative impact of each parameter on the uncertainty of the ICER estimate. Uncertainty around risk of death due to chronic HBV infection and risk of perinatal transmission had the greatest impact on the total variation in the ICER for deaths and infections averted. Higher risk of death from chronic HBV and higher risk of perinatal transmission resulted in increasing cost-effectiveness of a universal program.

Figure 2 shows the result of sensitivity analyses to evaluate the impact of different scenarios and assumptions related to the performance of the healthcare system on the ICER. The estimated coverage of HBVsAg screening during ANC had the highest impact on the ICER, and the higher the rate of antenatal screening, the more cost-effective the universal vaccination strategy becomes. Across the range of scenarios considered by the sensitivity analyses, including the most optimistic and pessimistic assumptions for the performance of the healthcare system in implementing these programs, selective screening was only the more cost-effective alternative if costs associated with rapid HBsAg testing are assumed to be negligible. Even if the service delivery costs of antenatal rapid HBsAg testing are completely disregarded, the incremental cost of a universal birth dose program would be US$509 per additional HBV death averted, which is highly cost-effective given that the GDP per capita for STP in 2014 was $1,811 [29].

Discussion

Our assessment of the HepB-BD program in STP revealed a high degree of uniformity and quality in the implementation of selective HepB-BD vaccination in STP. HepB-BD messaging during antenatal care is strong and consistent, with HBsAg-positive mothers strongly counseled to seek facility births and obtain immediate HepB-BD if an unplanned home birth occurs. Although timeliness was not recorded or reported, all interviewed staff reported that in practice the dose was administered moments after birth in all routine facility births.

Nevertheless, we identified several shortcomings in the program. Data recording and reporting policies and practices should be modified and strengthened to ensure that timely vaccination coverage of all eligible infants can be calculated and monitored at a district and national level. In addition, the practice of withholding breastfeeding initiation until HepB-BD administration is not supported by existing recommended policy [1,5], and risks leading to unnecessary delay in breastfeeding, with possible consequences for neonatal mortality [30]. Finally, there is a clear need for standardized policies and procedures for HepB-BD to be created and disseminated to practitioners in all maternity facilities.

The principal reason for not providing HepB-BD to all newborns was the selective vaccinate policy. Given the high coverage of antenatal care (97.5%) and the high proportion of facility births (91%) in STP [9], a fairly high HepB-BD coverage of at-risk infants can be estimated, consistent with the 92% coverage of at-risk infants estimated by the MOH. However, our study found that this strategy results in fewer prevented chronic HBV infections and HBV-related deaths, at nearly double the cost of a universal vaccination approach.

We chose an incremental approach to estimating costs, as information about the incremental cost of an alternative program is most useful to decision-makers in the ministry of health. However, this approach relies on the assumption that the existing health system is functioning adequately with capacity to expand to universal vaccination without requiring new capital investment in shared vaccine program infrastructure, or significant increase in staff. This assumption may not be valid in many developing country settings with baseline shortage of healthcare personnel, so the results should be interpreted with that caveat in other countries.

There are several limitations in the economic analysis. First, we did not model the risk of horizontal transmission; though data on the impact of birth-dose on horizontal transmission are highly limited, our estimate most likely underestimates the impact of birth dose vaccination under a universal vaccination policy by not accounting for reduced horizontal transmission in the first 6 weeks of life. Additionally, we did not use a dynamic transmission model to incorporate the protective impact of herd immunity. We also focused on births that occur in maternity facilities, and assumed that no outreach services would reach infants born at home. Many of the model parameters were sourced from secondary data, introducing uncertainty to the findings. For example, cost data for service delivery for vaccination and rapid testing are not available from STP, therefore we used data from Benin and Cote d'Ivoire [20,22]. As these West African countries are economically similar (PPP-adjusted GDP per capita in 2014: 3176-STP, 3258-Cote d'Ivoire, 2030-Benin), these are reasonable proxies. Sensitivity analyses to explore a wide range of costs, transitional probabilities, and assumptions revealed a robust finding of substantial cost savings per HBV-associated death averted under a universal vaccination program regardless of the uncertainty in model parameters. Finally, we calculated ICER in terms of US$ per chronic infection prevented or HBV-related death prevented, rather than in terms of disability-adjusted life years (DALYs) gained or lost, which could be interpreted in a willingness-to-pay context (typically a DALY-based ICER smaller than the GDP per capita is considered highly cost-effective). However, as we found that switching to a universal vaccination strategy would result in an incremental cost *savings* per death

averted under all but the most extreme cost assumptions, the acceptability of a universal vaccination model is assumed to be greater than the base-case model.

The HepB-BD program in STP, which we found to be of high quality and currently ensures high coverage of timely HepB-BD, can be further strengthened by developing written national policies and conducting training of staff to ensure uniform implementation of the program according to accepted standards. Additionally, our assessment and model determined that that adopting a universal vaccination policy in line with WHO recommendations would be lower cost and more effective, less likely to miss children at risk for HBV infection, and would be simpler to implement than the existing selective vaccination program in STP.

Acknowledgements

We are grateful to the immunization staff and health care workers who offered their time to participate in this survey in order to help improve birth dose vaccination in STP.

Table 1: Facility characteristics and hepatitis B birth dose (HepB-BD) vaccine knowledge, practices, and vaccine management. São Tomé and Príncipe, 2015

	All facilities (n=5)	National public hospital (n=1)	District public hospital (N=3)	Health center (N=1)
Background characteristics				
Total number of deliveries (median [range])	336 [31-4383]	4383	336 [177-357]	31
100% of mothers stay >=24h post delivery	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Knowledge				
Received training on HepB-BD	4 (80%)	1 (100%)	3 (100%)	0 (0%)
Know that a mother can transmit HBV to her baby	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Know that recommended HepB-BD administration is <24h of birth	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Practices				
Vaccinate ALL newborns with HepB-BD	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Follow standard written protocols for HepB-BD administration	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Provide written documentation of HepB-BD to mother	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Vaccinate in the delivery room	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Administer to low weight babies (2-2.5 kg)	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Administer to very low weight babies (<2kg)	4 (80%)	1 (100%)	3 (100%)	0 (0%)
Administer to premature babies	3 (60%)	1 (100%)	2 (67%)	0 (0%)
Administer to unstable babies	1 (20%)	0 (0%)	1 (33%)	0 (0%)
Provide HepB-BD outreach vaccination to home births	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Charge patient for HepB-BD administration	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Patients sometimes refuse HepB-BD	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Offer HepB-BD daily	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Require a physician order for HepB-BD	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vaccine management				
Stockout >2 weeks in 2014	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vaccine fridge is EPI-approved	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Observed VVM stage 3-4 in fridge	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fridge is monitored at least 2x/day	5 (100%)	1 (100%)	3 (100%)	1 (100%)
Vaccine is obtained from MOH EPI	5 (100%)	1 (100%)	3 (100%)	1 (100%)

Table 2: Modeling assumptions and parameters for decision analytic model of hepatitis B birth-dose immunization cost-effectiveness. São Tomé and Príncipe, 2015.

Parameter, reference number	Base-case point estimate*	Range	Sensitivity range	Source
Vaccine and rapid test performance				
Effectiveness of HBV BD vaccine	88.0	50.0—95.0	–	[3,15]
HBV test sensitivity	98.2	94.7—99.0	–	[16]
HBV test specificity	99.9	99.3—100	–	[16]
Perinatal transmission risk				
Transmission risk for HBVe positive mothers	49.6	9.2—90.0	–	[3,17]
Transmission risk for HBVe negative mothers	15.3	1.8—28.7	–	[3,17]
Disease model				
Transmission to symptomatic acute infection	0.01	0—0.08	–	[3,18]
Symptomatic to acute fulminant infection	0.1	–	–	[3,18]
Acute fulminant infection to death	70.0	–	–	[3,18]
Acute perinatal infection to chronic infection	88.5	84.0—94.0	–	[3,17]
Chronic infection to HBV-attributable death	25.0	10.0—40.0	–	[3,19]
Costs				
Unit cost of vaccine	$0.38	–	$0.00—0.76	UNICEF price sheet
Costs of HepB-BD (selective)	$0.28		$+/-100%	[20]
Cold chain maintenance	$0.01			
Program management	$0.02			
Record keeping	$0.11			
Routine facility-based service delivery	$0.07			
Supervision	$0.04			
Surveillance	$0.03			
Additional per-dose costs of universal program	$0.54		$+/-100%	[20]
Training	$0.05			
Other	$0.05			
Advocacy and social mobilization	$0.44			
Unit cost of rapid test kit	$0.95	–	$0.00—1.90	Market purchase price for Sao Tome**
Nursing time required for test (minutes)	17.5	–	8.8—26.3	[21,22]
Nursing time required for post-test counseling (positive test)	22.5	–	16.9—33.8	[21,22]
Nursing salary per hour	$1.89	$1.69—2.10		[22] (uses inflation-adjusted Cote d'Ivoire and Comoros as range)
Epidemiological assumptions and health system parameters				
Birth cohort	6385	–	–	[6]
Rate of stillbirth in STP	1.6	–	–	[13]
Maternal prevalence of HBsAg	6.1	5.2—7.1	–	[7].
Prevalence HBeAg among HBV positive mothers	30.6	15.5—41.1	–	[23]
Overall facility birth proportion	91.0	88.8—93.2	–	[9]
ANC coverage (at least 1 visit)	97.5	96.2—98.7	–	[9]
Timely BD coverage among hospital births	92	–	80—100	National surveillance data (% coverage of hepatitis B-positive mothers used as a proxy)
Timely birth-dose coverage among home births	0.5	–	0—100	Author's assumption
Rate of screening for HBsAg if ANC	0.95	–	80—100	Author's assumption
Percent of mothers without ANC who seek	0.75	–	50—100	Author's assumption

hospital births				
Probability of rapid test for a facility birth who did not receive ANC	0.8	–	50—100	Author's assumption

*When a range was available in the literature, as base-case estimate the mean value was chosen.

**Communication with Luis Manuel do Sacramento Bonfim, Health Specialist, UNICEF São Tomé and Príncipe.

Table 3: Monte Carlo estimates from decision analytic model of hepatitis B birth-dose immunization cost-effectiveness. São Tomé and Príncipe, 2015.

Modeled HepB-BD vaccination approach	Number of annual infections	Number of chronic infections	Number of HBV deaths	Cost per year (in 2015 US$)	Incremental cost-effectiveness ratio (US$ per chronic HBV infection averted)	Incremental cost-effectiveness ratio (US$ per HBV-related death averted)
Universal vaccination	24 (14—40)	21 (13—35)	5 (3—10)	6,870 (6,824—6,915)	NA	NA
Selective vaccination	29 (19—45)	26 (17—40)	6 (3—11)	12,311 (11,885—12,736)	1,234 (819—1,880)	5,012 (2,901—9,239)

Base-case estimates and 95% confidence interval calculated by reporting the 50th, 5th, and 95th percentile of 10,000 Monte Carlo iterations of the decision analytic model. Estimates are rounded to the nearest whole. A positive value for incremental cost effectiveness ratio is interpreted as cost-savings if a universal vaccination strategy is adopted.

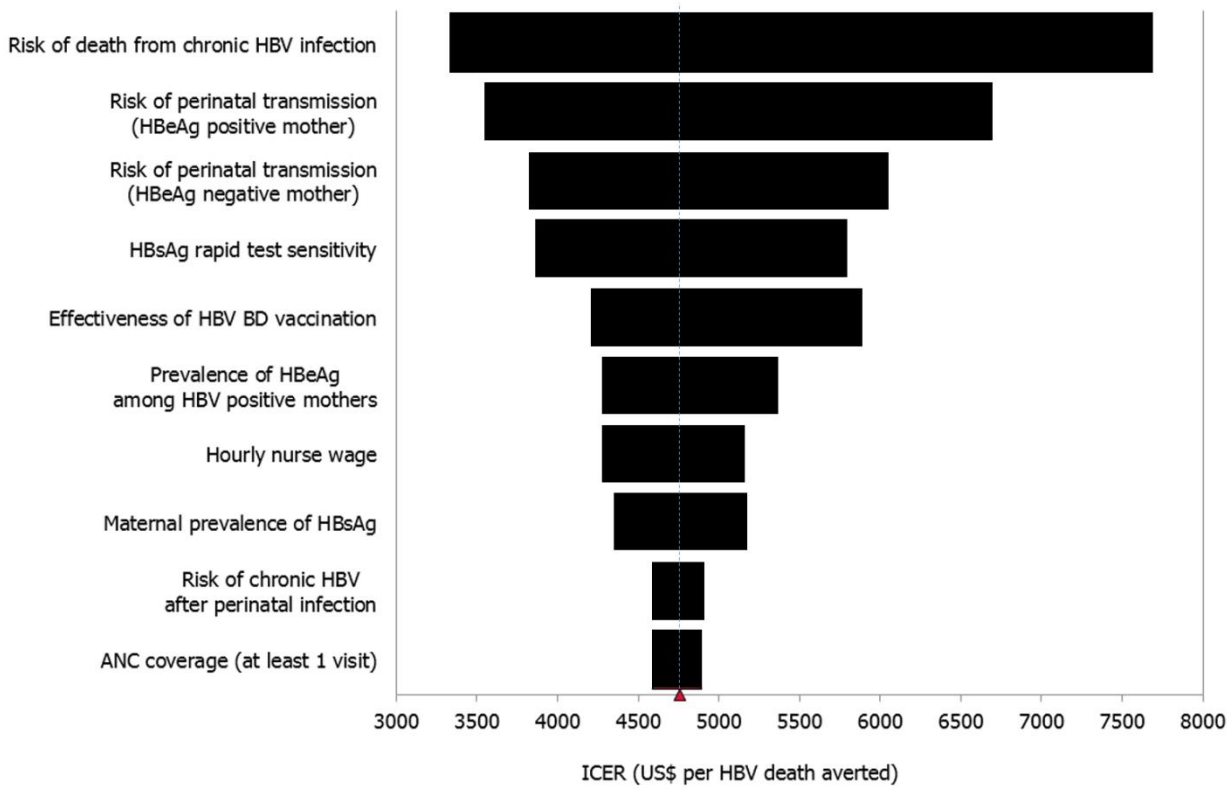


Figure 1: Tornado plot of stochastic sensitivity analysis accounting for parameter uncertainty. Parameters on the y-axis are ranked by their effect on the median ICER estimate after 10,000 simulations. Range of bars indicates the impact on the 50th percentile of Monte Carlo simulation results across the range of possible values for each parameter. Positive ICER indicates higher cost effectiveness of a universal vaccination program.

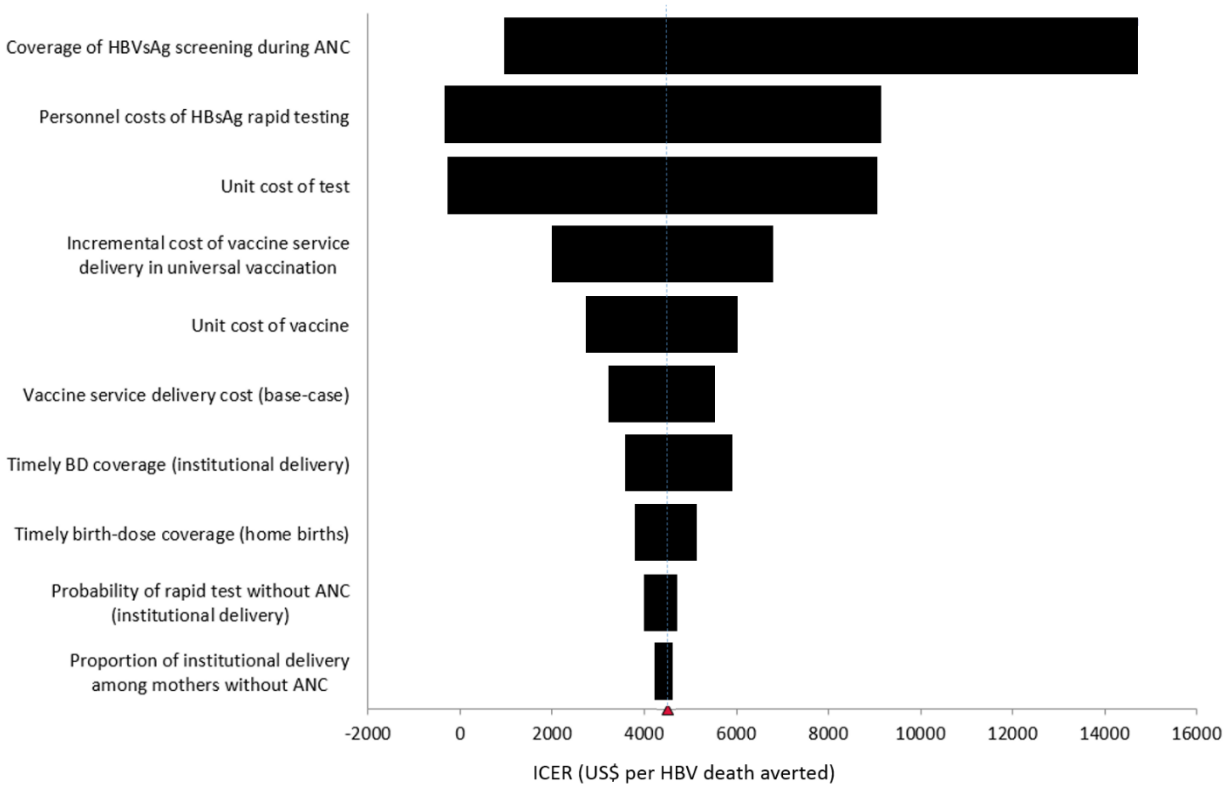
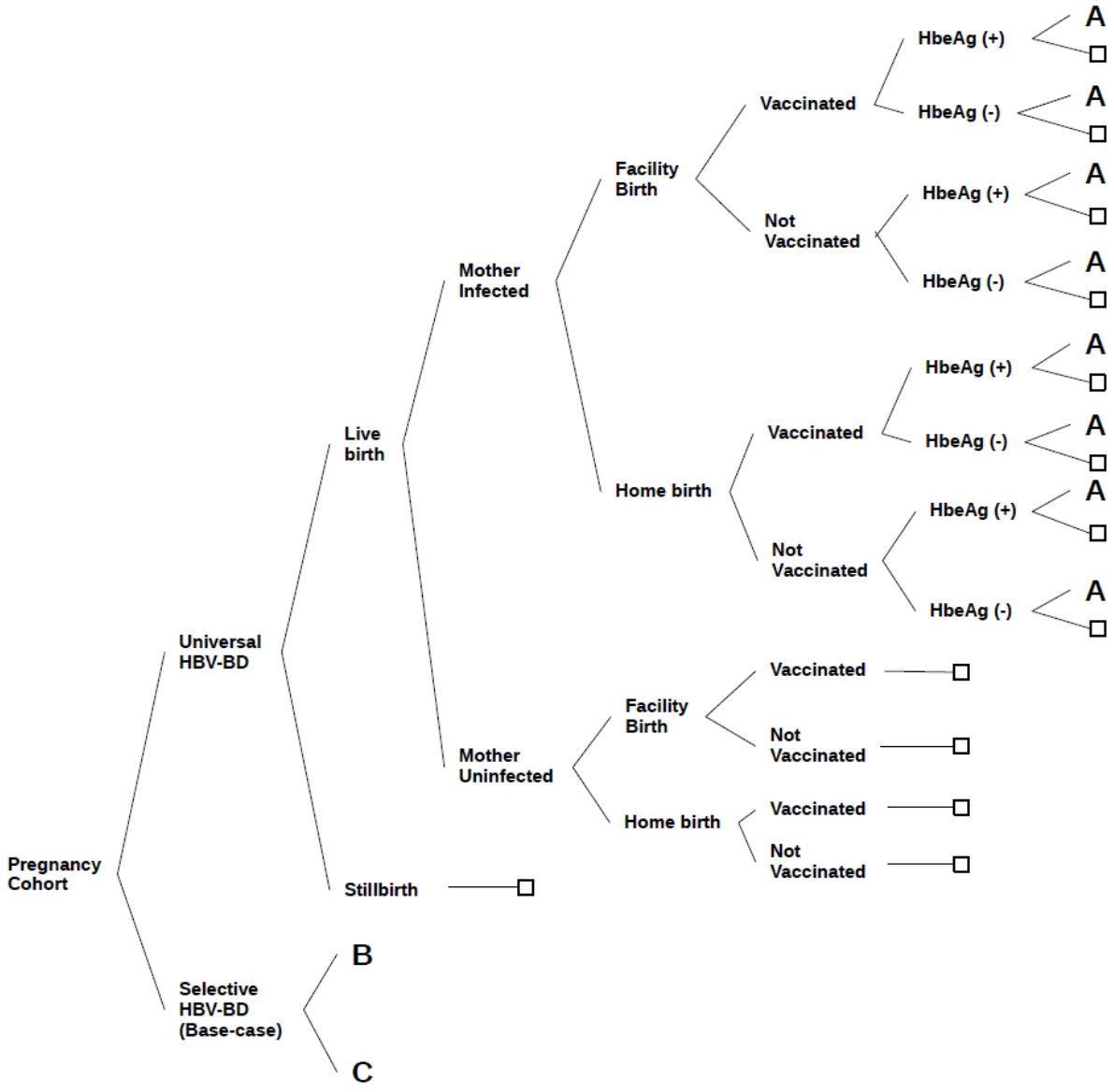
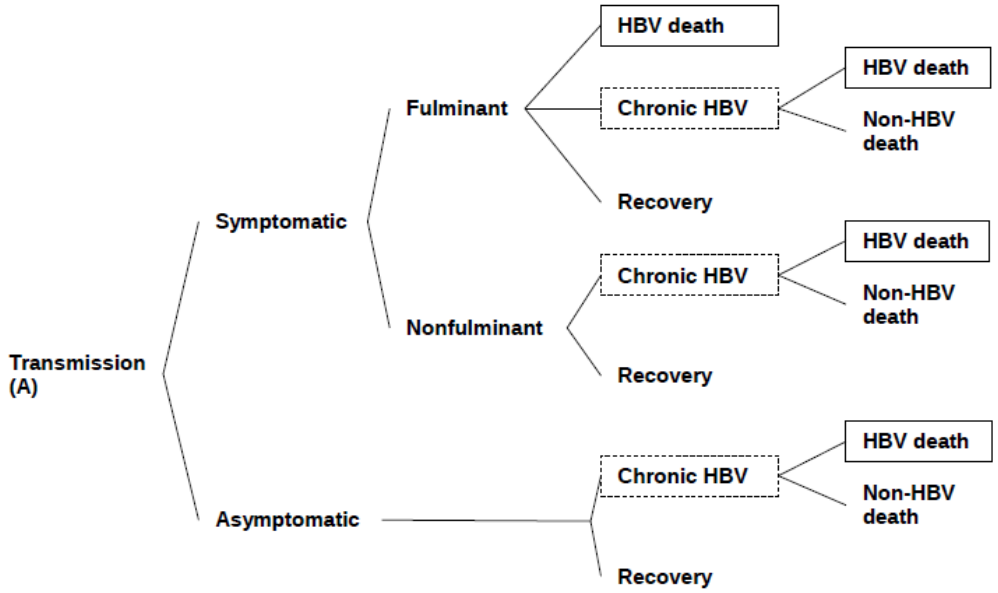
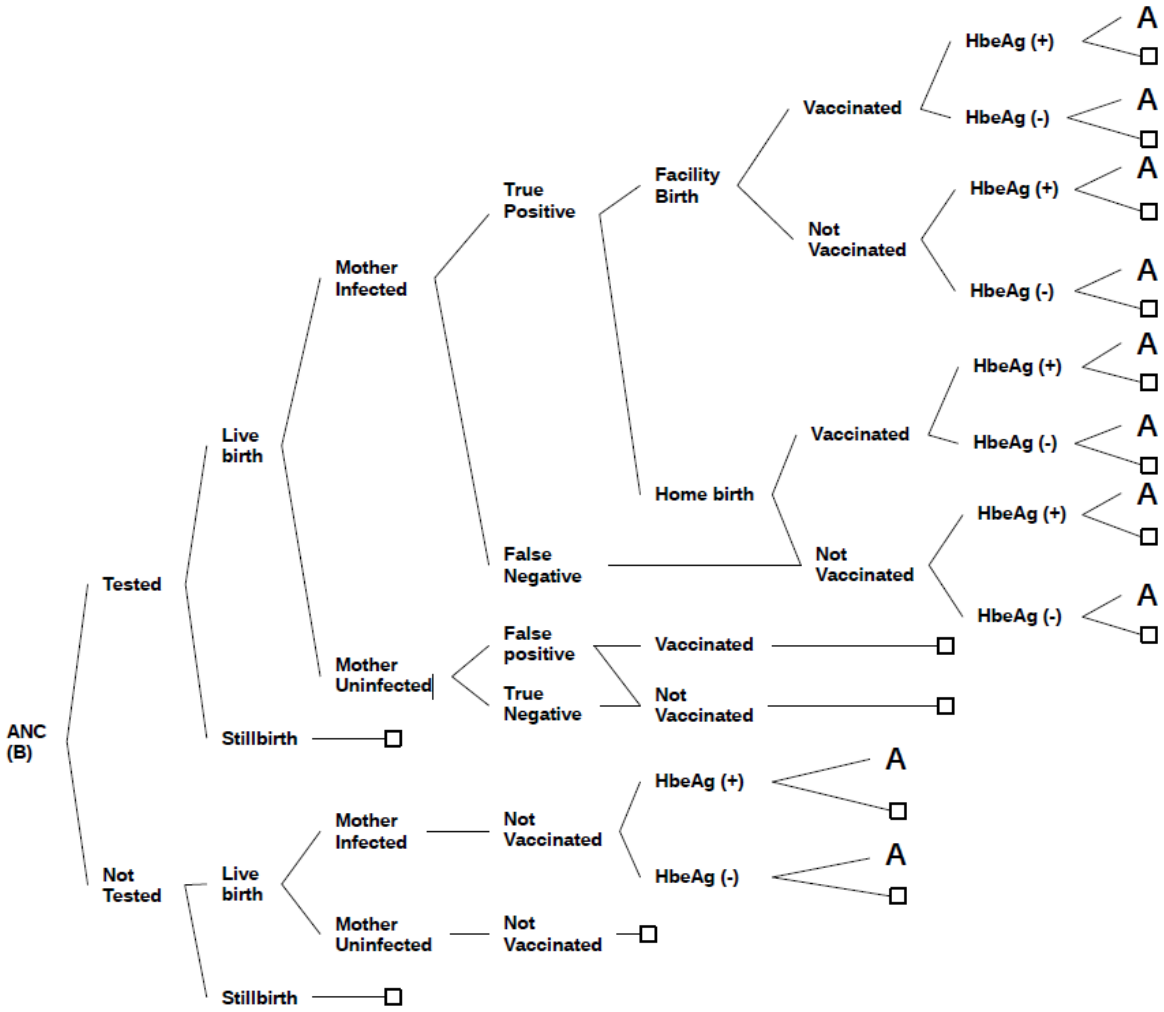


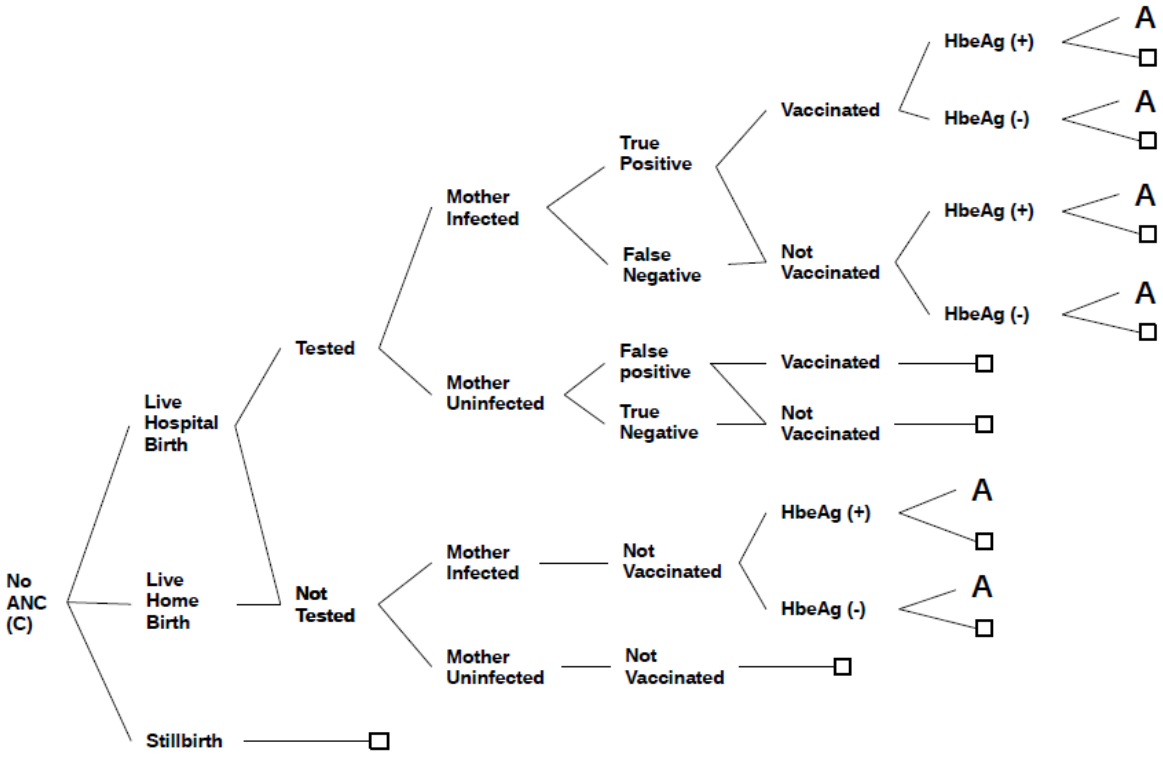
Figure 2: Tornado plot of sensitivity analysis evaluating the impact of different scenarios and assumptions on the incremental cost-effectiveness estimate. Parameters on the y-axis are ranked by their effect on the median ICER estimate after 10,000 simulations. Range of bars indicates the impact on the 50th percentile of Monte Carlo simulation results across the range of possible values for each parameter. Positive ICER indicates higher cost effectiveness of a universal vaccination program.

Appendix A: Decision analytic tree used to calculate costs and effects of two alternative strategies for providing hepatitis B birth-dose in São Tomé and Príncipe. Open boxes=No infection.




Transmission (A)
Symptomatic
Asymptomatic
Fulminant
Nonfulminant
HBV death
Chronic HBV
Non-HBV death
Recovery


ANC (B)
Tested
Not Tested
Live birth
Stillbirth
Mother Infected
Mother Uninfected
True Positive
False Negative
False positive
True Negative
Facility Birth
Home birth
Vaccinated
Not Vaccinated
HbeAg (+)
HbeAg (-)
A


No ANC (C)
Live Hospital Birth
Live Home Birth
Stillbirth
Tested
Not Tested
Mother Infected
Mother Uninfected
Mother Infected
Mother Uninfected
True Positive
False Negative
False positive
True Negative
Not Vaccinated
Vaccinated
Not Vaccinated
Vaccinated
Not Vaccinated
HbeAg (+)
HbeAg (-)
HbeAg (+)
HbeAg (-)
HbeAg (+)
HbeAg (-)
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