Thesis


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Background
The Hepatitis B Virus (HBV) is a blood-borne infection affecting around 2 billion people at any given time and is commonly transmitted through Mother to Child Transmission (MTCT). Preventative measures include vaccinations, particularly the timely Birth Dose (TBD) given within 24 hours of birth. Timing is crucial for the efficacy of the TBD, and is influenced by various factors. São Tomé and Príncipe is one of seven sub-Saharan African countries with a TBD policy. This study aims to observe the different proportions of children receiving adequate or inadequate vaccinations against HBV, as well as to analyse the risk factors that may lead to inadequate vaccination.

Methods
Secondary data from the São Tomé and Príncipe Demographic Health Survey from 2008-2009 was analysed in this study. Dose delays for all children and those at risk were described. An associative analysis looked at the potential risk factors for inadequate TBD vaccination.

Results
A high coverage rate for vaccinations was found (>85%), however, the majority were delayed, with only 1% and 4% on time, and mean a TBD administration of 2(SD±2) months after birth, in all children, versus children at risk. Children born to mothers with positive HBV status and low wealth were significantly more likely to receive the TBD on time.

Conclusion
The majority of vaccinations, including the TBD were inadequately administered, denoting a concern of transmission to children born at risk. Additionally, socioeconomic factors were found to be factors influencing the provision of the TBD
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**Abbreviations**

HBV: Hepatitis B virus  
HBV+: Hepatitis B virus positive  
TBD: Timely Birth Dose  
MTCT: Mother to Child Transmission  
WHO: World Health Organisation  
DHS: Demographic health survey  
SSA: sub-Saharan Africa  
AFRO: African Health Observatory for the WHO  
HIV: Human Immunodeficiency Virus  
DOB: Date of Birth
**Introduction**

In 2016, the WHO adopted the Global Health Sector Strategy on Viral Hepatitis 2016-2030, with the vision to eliminate hepatitis as a major public health concern globally\(^1\). The Hepatitis B virus (HBV) is a blood borne virus which is transmitted interpersonally through sexual and non-sexual contact, from mother to child transmission (MTCT) and through infusion with infected blood products. The repercussions of HBV revolve around chronic infection, which results in liver pathologies such as cirrhosis and hepatocellular carcinoma\(^2\). Viral hepatitis has been estimated to be responsible for 1.45 million deaths in 2013, of which 47% is accountable to HBV\(^3\).

In newborns, protection in the form of providing immunisations against HBV has been a vital aspect of preventing vertical transmission. The recommended immunisation schedule comprises commonly of 3 to 4 injections, paramountly with the first timely birth dose (TBD), which prevents an estimated 80-95% of transmissions if given within 12-24 hours of birth\(^5\). Delaying or missing the TBD drastically increases the chances of MTCT. With an increasing interval between the time of birth and receiving the TBD, the efficacy of conferred protection from active immunity is known to be reduced\(^6,7\) and the same effect, to a lesser extent is apparent with the latter two doses\(^8,9\). Additionally, delaying or missing the first dose increases the risk of missing or delaying the rest of the vaccination series\(^8\). Given the efficacy of this universal HBV vaccine schedule, it has been incorporated into various newborn immunisation programmes around the world, and has been heralded as a key strategy by the WHO, especially in resource limited settings\(^1\). The African Health Observatory sector of the WHO (AFRO) have recommended different guidelines regarding the first dose, allowing it to be given after 1 month from birth in countries within this region\(^10,11\). However, despite these efforts and recommendations, not all children in the world receive the full vaccination sequence (82%), and even fewer receive the crucial birth dose (38%)\(^1\). This is reflected within the Africa region, where all 47 states have adopted some form of the vaccination series, with a vaccination coverage rate of 77%, but few countries have uptaken the TBD, with a
TBD coverage rate of 11%\textsuperscript{12}.

The sub-Saharan Africa (SSA) region has one of the highest hepatitis mortality burdens in the world, with an estimated 5-8\% of the population infected\textsuperscript{4}. It has been argued that the majority of transmissions occur through horizontal transmission from person to person rather than vertical transmission from mother to child, i.e. MTCT\textsuperscript{5}. This is contrary to what is thought to be the most prevalent mode of transmission in other endemic countries, where MTCT is focused heavily upon by public health strategies.

**Risk factors for missing the Timely Birth Dose**
The TBD is recommended to be given within 24 hours from birth. It is therefore important that not only the policy exists to instruct healthcare professionals to vaccinate at birth, but it is feasible to do so. Many factors influence the efficacy as well as the feasibility of the TBD, such as maternal, environmental, socioeconomical, cultural and health system factors. The hypothesised relationship between these and MTCT are displayed in the conceptual framework in figure 1, below.

Maternal socioeconomical factors are key determinants of access to vaccination\textsuperscript{13}, and its relationship to the provision of the TBD is complex. Poor financial status is a barrier to some mothers when accessing vaccination services in some countries\textsuperscript{14}, as well as to healthcare providers\textsuperscript{15}. Outside of the cost of these vaccination services, wealth affects an individual’s educational level, place of residence and other practical and environmental factors important in the provision of the TBD and vaccinations against HBV.

The maternal place of residence can have an effect on birth practices, and thus the provision of TBD delivery. Rural areas may subject individuals to poorer healthcare access, especially with regards to birth notification and tracking, compared to urban areas\textsuperscript{16-20}. There are therefore challenges in achieving adequate birth attendance by skilled assistants, as well as access and transport to facilities for the safe provision of birth giving. In addition, residence in a rural area may indicate a lower socioeconomical status.
It has been shown that an increased awareness and knowledge of HBV and its risks results in better outcomes in vaccination\textsuperscript{21,22}. Demand for, and adherence to the vaccination schedule increases with better knowledge and information\textsuperscript{23}. Literacy comprises a component in this understanding, influencing a mother’s ability to access and adhere to recommended vaccination practices\textsuperscript{24}. Knowledge of the HBV is variable amongst populations. A study in Ghana\textsuperscript{15} amongst 209 pregnant women revealed that although the majority of individuals had heard of HBV before, only half were unaware of the repercussions, and that it could be passed to their children via MTCT. Knowledge was not only lacking in regards to the repercussions, but additionally over half were unaware it was transmitted through sexual contact. In the short period after birth, clear understanding of the TBD is crucial for implementation. Importantly, low education and literacy level, is yet again suggestive of low socioeconomical status.

The coverage by health insurance of a mother is known to increase newborn TBD vaccination rates, aiding with the potential financial costs of vaccination and birth\textsuperscript{14}. The acquisition of health insurance coverage is dependant however, on maternal wealth, and in itself, is an indicator of socioeconomical status.

The place of birth is a practical factor that influences the provision of vaccination administration. Mothers who give birth in hospitals are more likely to have their children receive the TBD. Studies in China have shown that increasing the number of births in hospitals increases the overall TBD coverage rate in newborns\textsuperscript{20}. Another aspect to be considered is the type of facility that mothers give birth in. Giving birth in private facilities has been shown to result in lower rates of TBD coverage, owing to poor knowledge, supervision and financial charges\textsuperscript{14,18,19,25}. Irrespective of the type of healthcare facility at which the baby is born, there exists a plethora of factors that determine the feasibility of a timely birth dose. For instance, the location of vaccination services is key to the timely provision of this intervention, particularly, whether the service is offered at the site of birth, or off site. On-site delivery of vaccination services has been shown to be associated with higher TBD coverage in a study conducted in Cambodia. Moreover, variances in vaccine practices were also a factor, with TBD delivery being higher if given on the
maternity ward, compared to other departments\textsuperscript{16}.

Delivery by caesarean section has been argued as a method of preventing HBV MTCT. Although it is not a risk factor for missing the TBD, caesarean rates may give an indication of pre-existing knowledge of HBV status in the mother, which aids in the timely vaccination of their children\textsuperscript{26}.

The screening of pregnant women is a key strategy in delivering targeted care and follow up of mothers and their children, however it is normally an approach reserved for higher income settings\textsuperscript{27}. Pre-existing knowledge of maternal HBV status increases TBD coverage\textsuperscript{23,28-30}. Universal or targeted screening as a strategy compared to universal TBD vaccination is more costly and less effective, especially in the latter form. In a survey of 36 physicians from Ghana, over one third were willing to test for HBV status in women, however cost and time restraints were cited as reasons for preventing them in doing so\textsuperscript{15}.

Finally, Human Immunodeficiency Virus (HIV) coinfection with HBV is a concern that affects a proportion of infected individuals\textsuperscript{31}. HIV has been suggested to have a role in decreasing the efficacy in vaccines in infants, although more evidence is needed\textsuperscript{9}. HIV comorbidity may have an influence in alerting healthcare professionals about maternal HBV status and thus to aid in the screening process.

Other than maternal and health facility level factors, logistics play a role in TBD vaccine delivery. Supply shortages in dose stores both locally and nationally are detrimental to any plans for vaccination\textsuperscript{16}. Additionally, due to the temperature volatility of vaccine doses, the requirement of cold-chain storage poses a logistical dilemma for healthcare professionals out in the community\textsuperscript{17}. The HBV vaccine is more expensive than others included in national immunisation programmes thus, in lower resource settings, lower wastage rates are important for the efficiency and sustainability of HBV vaccination. In Indonesia it was demonstrated that, in comparison to 10-dose vaccines that were cheaper, the usage of mono-dose vials resulted in higher TBD coverage\textsuperscript{17}. This is because communities that only had one or two births in a given visit by a community birth assistant, there was more hesitance and thus less usage of the 10-dose
HBV viles, as this usually led to wastage.

Between the different settings around the world, various cultural beliefs and practices affect the delivery and effectiveness of the TBD. In China and Indonesia for example, certain families keep newborns at home for at least a month, reducing the chances of timely vaccination\textsuperscript{17,19}. In an issue less cultural and more health professional orientated, vaccinators wait for at least several hours before giving the TBD in Viet Nam and Indonesia, due to fear of blame in adverse newborn outcomes\textsuperscript{17,18}.

**Rationale**

São Tomé and Príncipe is one of only seven SSA countries to have implemented a HBV TBD vaccination policy into its immunisation schedule, since 2005\textsuperscript{32}, thus it is important to observe its impact in the general population, and also in those at risk. Additionally, it is known that despite whether being featured in national immunisation schedules or not, certain barriers can prevent or delay the vaccination of a newborn. The reasons for this deficit in coverage is multifactorial, involving environmental, socioeconomical and health facility level factors. It is therefore vital to assess the impact of this national immunisation strategy, and to consider the implications of introducing it to other SSA contexts.

**Aims**

The primary outcome of this study was to observe and describe the frequencies and distributions of vaccination inadequacies, particularly those born to HBV infected mothers at higher risk of MTCT, in a population from São Tomé and Príncipe. The aim of this outcome was not to compare the risk of transmission between those at risk and those of the general population, but to give a general overview of risk for these demographics. The predictive variables are the maternal HBV status and time from birth to vaccination, yielding the outcome of proportions of children with inadequate vaccination (missed or delayed TBD and doses 2 and 3). Alongside this, the secondary aim of this study was to analyse the associations that may be risk factors for incomplete TBD vaccination in newborns. This associative analysis may give an insight into the shortcomings as well as the effectiveness of the national immunisation programme for the
population of São Tomé and Príncipe.

**Research question**
What proportion of children in São Tomé and Príncipe, particularly those born to HBV infected mothers, are at higher risk of contracting Hepatitis B, and what are the associated risk factors for inadequate Hepatitis B timely birth dose vaccination, between 2008 and 2009?

**Figure 1: Conceptual Framework demonstrating possible outcomes and risk factors for a child born to a hepatitis B positive mother (HBV+).**
Materials & Methods

Study design

This study was an observational analysis using secondary data from the Demographic and Health Survey (DHS) program of São Tomé and Príncipe, 2008. The DHS is a cross-sectional health and demographic surveillance survey of households and individuals conducted nationally, in 90 various low to middle income countries. The DHS is implemented by ICF international, and funded by the United States Agency for International Development (USAID), a governmental agency, as well as other donors. The primary outcome of this study was ascertained through use of descriptive analytical methods on this data. Prevalence of HBV positive mothers and children with missed or delayed vaccinations were observed in order to estimate the proportion of children at risk of infection. Vaccination statuses of all children were stratified and described, in addition to this. Increased risk of MTCT in this study was defined by inadequate vaccination. The secondary outcome of this study involved an associative analysis of a range of exposures suspected to be risk factors for missing or delaying a dose in the infant vaccination schedule.

Study setting

The survey includes a representative sample of the population from all regions on both islands of the nation, conducted between September 2008 to January 2009. The two main islands of São Tomé and Príncipe are amongst an archipelago of smaller islands belonging to the nation, surrounded by the Atlantic Ocean and the Gulf of Guinea. This geographical constitution makes the island nation a unique setting to study, having implications on healthcare access, transport and commercial factors. Across the sea, the islands are bordered by Nigeria to the north, Cameroon to the north east and Gabon to the east, amongst other SSA nations on the west coast of central Africa.

As part of DHS sampling protocol, once census data was taken in order to define sampling frames, up-to-date household listings were constructed and data collection commenced within six months.
**Study population**

Participants were acquired through periodic 2 stage cluster sampling from a cross section of the population, ensuring national representativeness\(^{35}\). The final sample population the DHS survey was able to capture consisted of 3536 households, which included 2615 women aged 15-49 and 2296 men aged 15-59, and further to this, 7620 children of all ages were also registered (of which, 1928 were born within 5 years of the survey), making a total of 13430 household individuals. This is in the context of a national total population of 197,541\(^{36}\) within São Tomé and Príncipe, thus the sample population was 6.8% of the overall population it was representing. These figures are demonstrated in figure 2. Figure 2 is a conceptual map which details the participant flow into the subpopulations required according to the primary and secondary outcomes of the study.

Within a listed household, different members were eligible for different surveys. The DHS household survey identified men, women and children of the appropriate age who were eligible for various questionnaires.

To analyse this secondary data, the study sample was achieved through filtering the overall sample population through a set of criteria, displayed for reference in figure 2. Firstly, from the broader population of women, those who were HBV positive were included, and then those with children from the past 5 years were further specified for up to three children per mother. This was because data for HBV vaccination were only available in these children. No women had more than three children in the specified period. All children born to these mothers were assessed for inadequate vaccination schedules and were placed in one of three categories; 1. If they had missed or delayed the TBD 2. If they had missed or delayed the second dose and 3. they had missed or delayed the third dose. This provided the population to be described for increased MTCT risk. In addition to this population, all children described in the survey were isolated for descriptive analysis. All children were included in order to ascertain the general transmission risk for this demographic, irrespective of maternal HBV status. Thus in the second group, children at risk were also included. Exclusion criteria consisted of all men who partook in the survey, and women who had not given birth within 5 years prior to survey
conduction. Women who had missing values for the hepatitis B test were excluded from both subpopulations and HBV negative women excluded from the subpopulation for analysis of high-risk infants. Furthermore, women who had not given birth within 5 years, from the hepatitis B positive group were excluded.

For the secondary outcome, all children born within 5 years to women were defined and their TBD immunisation statuses were stratified. Likewise, children who had missing vaccination data were excluded.

Figure 2: Flow diagram showing conceptual flow of participants and risk factors for secondary outcome with inclusion criteria, according to Primary and Secondary outcomes of study.
Variables
The primary outcome; the proportion of children at risk of MTCT was indicated by the prevalence of hepatitis amongst mothers- according to their HBV blood test results. The main predictor, delay in vaccinations, was given as number of months (mm) and was ascertained by taking the vaccination date for each dose (first, second and third or, lack of), their month and year of birth, and calculating the number of months between the two, giving the number of months transpired. For example, if the DOB variable was 0706 (mmyy) and the vaccination date was 1206 (mmyy), the delay variable would have been 03 months. The type of vaccination inadequacy (or delay) of children was categorised according to the criteria outlined in the previous section above. The time frame for which the TBD is to be ideally given was defined as within 24 hours after birth\textsuperscript{11}, however, due to the lack of data for the day of the child’s birth, delayed TBD was defined as a delay of one month. This definition, along with the second and third doses, advised to be given at 10 and 14 weeks after birth, are recommended by the AFRO division of the WHO\textsuperscript{10,11}. Delayed second and third doses were defined as vaccinations given after 3 and 4 months after birth.

The secondary outcome of this study was indicated by examining exposure variables collected from the DHS “individual” questionnaire, taken by women. The variables were deduced to be various risk factors identified as causes of poor infant immunisation coverage in a literature review conducted in November 2016\textsuperscript{37}. The association of these factors are demonstrated in the conceptual map in Figure 1, and are listed in Table 1, in the Annex. These factors were contracted from various maternal, health system and environmental barriers. For this population, children were grouped according to TBD vaccination only. The two groups comprised of those children who received the TBD without delay, and those who either received the TBD after 1 month or missed it completely.

Data Cleaning and Variable Management
The recoded dataset containing the responses for all the individuals who answered the DHS individual questionnaire was used for this study. The data collected responses for hundreds of questions, of which the vast majority were not required for the use of this study. As a result, little under 30 variables were kept for processing within the SPSS statistical software. Each case
contained a mother’s responses to these variables and within these responses; details of up to 3 of her children were included. In order to process the details of these children individually, the recode file was processed in a way which allowed for all children within the study to be recognised as individual cases, with corresponding maternal factors included. This was handled by a combination of data management tools within SPSS and Microsoft Excel 2010. In addition, recoding of certain variables was necessary and carried out using SPSS. The details of these recodings are displayed in table 2, in the Annex and involved a mixture of category merging (such as the variable containing place of delivery) and deletion of categories with no responses.

**Statistical methods**

Descriptive methods were used to observe the vaccination statuses of the children. SPSS software (IBM, version 20) was used for processing and statistical analysis of the data. Despite the unavailability of childhood HBV status within the data, a percentage of children without adequate vaccination schedules, born to HBV positive mothers could be assessed and stratified for higher risk of transmission. As well as frequencies, descriptive distributions were calculated showing means and standard deviations of vaccination delays.

Associative analysis was performed on variables suspected to influence TBD dose adequacy. Two independent groups consisting of children who received the TBD on time and those who had missed or delayed the TBD were compared. Predictive variables consisted of maternal and environmental characteristics as outlined in the “variables” section above. Associations were tested using either parametric or non-parametric crosstab methods for nominal data, namely the Pearson’s Chi squared test and Fisher’s Exact test. The utilisation of either method was chosen based on the cell counts for the categorical variables. Cells with a frequency of >5 required the utilisation of Pearson’s Chi squared test, whilst Fisher’s Exact test was used for cell counts of <5. An alpha level of <0.05 was used to indicate statistical significance.

**Missing values**

Several variables which were to be examined for association with unmet vaccination adequacies were missing large amounts of responses or had no responses at all. These were identified in the
initial stages of variable analysis, and were removed from the dataset to be analysed. Variables were deemed to be worth analysing if they had fulfilled the requirement of having the response rate of 90%. These are detailed in the "Missing N/A" column of table 1, in the Annex.

With regards to the predictor variables concerned with the primary outcome (delay in vaccination), the day of birth was not collected by the DHS survey. This had a somewhat restrictive effect on the accuracy of the TBD delay calculation, with no differentiation between a delay of 1 day to over a month. For instance, if a child had received the dose on the second day after birth, according to the official guidelines, that child would have been categorised as delayed, however in this study, it would have been classed as “given on time”. Likewise, the same classification would have been given to a child vaccinated at 29 days. Despite this, the general distribution of vaccination timings and adequacies can be observed by using this data, and is still within the AFRO WHO division’s guidelines. This is examined further in the discussions section.

Some of the variables denoting the hepatitis B vaccination date (“Hepatitis vaccination- second last child” etc) in the second and third last children had up to one third of responses missing. This is because for each mother, not all had given birth to more than one child within the 5 year time frame. Thus, these were negligible during analysis.

**Confounding factors**

No variables were selected to control for confounders. Additionally, effect modification was not tested for. Adjustment for confounding is vital in research in order to discern the cause-effect relationship between factors and the measured outcome. Due to the close relationships between the measured factors in this study, confounding adjustment could have been implemented, however this was not seen to be viable due to the small subpopulation size. The results of this associative analysis were therefore meant as an indication of the general influence of socioeconomical factors on vaccination. Small subpopulation sizes reduce statistical power when adjusting for confounding, as the number of covariates for inclusion within models is reduced. This approach would have eroded the precision of statistical tests, blurring the reflection of true effect, within the results.
Bias
The DHS employs rigorous sample selection protocols in order to reduce selection bias. Firstly, instead of allowing the same interviewing teams to perform household listings and selection before data collection, the DHS employs separate teams to implement household listing and selection beforehand. This has been shown to limit biases in sample selection. In addition, commencing data collection within six months of the sampling process ensures timeliness and accuracy\textsuperscript{39}. The researcher for this study had no conflicts of interest in the conduction of this research.

Ethical Considerations
Ethical review and approval of the DHS survey was conducted by the Institutional Review Board of Macro International, which complied with the United States Department of Health and Human Services requirements for the “Protection of Human Subjects” (45 CFR 46)\textsuperscript{39}. In addition, the ethical committee in São Tomé and Príncipe approved the entire survey including Hepatitis B testing, prior to its initiation\textsuperscript{40}.

The data collected by the DHS program employed various means by which it could ensure ethical soundness. The following is extracted from the DHS survey manual\textsuperscript{41}.

Firstly, participant recruitment is dependent on written informed consent without coercion. Support and approval for recruitment is built upon by public relations activities prior to the data collection phase.

The aspect of staffing is also rigorously organised for ethical soundness. DHS teams were staffed by a supervisor and both female and male interviewers, in order to match for the genders of respondents. Additionally, staffs were informed on sensitive issues such as HIV and malaria. On the topic of HIV, once informed consent was given, staffs were trained to take blood samples and in the instance that this was not feasible, technicians were utilised. Data regarding HIV was anonymised, and efforts were made to ensure that identifiable information was deleted, and respondents were relayed to nearby counselling services if required. The questionnaire script was available in the major local languages in order to improve validity and reliability. This is because when interviewers translate questionnaires themselves, errors can form and the inherent meaning
of the original question could be changed.
Lastly, data quality is held as a paramount responsibility for DHS surveys. Multiple levels of supervision were employed in order to ensure respectful conduction of interviews, as well as accuracy and consistency. "Re-interviews" were conducted in order to validate and match previously collected responses from the same household, by staff from central offices. Furthermore, quality control teams were also employed to periodically check non-response rates and validity of data. Lastly, data was inputted twice, from all questionnaires, in order to compare and solve discrepancies.

**Results**

**Participants**
The final cohort of participants derived for the analysis of this study was selected from the initial 2615 women who were recruited for the DHS individual questionnaire. Figure 3 demonstrates the flow of participant inclusion and exclusion for the analysis of the primary and secondary outcomes. For the primary outcome of this study, two subpopulations were derived. 975 women who had not given birth within the past 5 years were excluded from the original 2615 women. This gave 1640 mothers, and from these, 1629 children were derived for analysis, after excluding 299 children who had missing vaccination data, from the total of 1928 children.
The second cohort for descriptive analysis included 135 women with positive results from the hepatitis B test. The rest who were excluded included 2413 women negative in this test, and a further 63 women with missing results, including 4 tests which were recorded as “indeterminate”. Of the 135 hepatitis positive women, 57 had not given birth to a child within the last 5 years and were excluded. This left 78 mothers with a total of 99 children who were at risk of hepatitis B at the time of birth. In order to give a descriptive analysis of vaccination status for these children, information about their immunisation schedules were required, thus children with missing data were excluded. These consisted of 12 for the TBD, and 13 for both the second and third doses of vaccine. This meant that 87-86 children were included for the final descriptive analysis for the primary outcome, which was to determine the proportion of children at risk of HBV transmission.
For the secondary outcome of this study; an associative analysis into the risk factors for
inadequate TBD vaccination, the same cohort of children with vaccination data were included, giving a total of 1629 children.

Figure 3: Flow diagram of number of participants (n) included and excluded for descriptive and associative analysis, from respondents of the DHS survey in São Tomé and Príncipe, 2008-2009.

* - Includes women who had “Indetermine” responses to hepatitis B test results variable.
Blue boxes: Included participants, Red boxes: Excluded participants.
Descriptive characteristics: Vaccination schedules

A descriptive analysis was performed in order to observe the adequacy of immunisation, calculated according to the month and year of birth and vaccination date of the TBD, as well as doses 2 and 3. The status of immunisation schedules were stratified for all 1629 children, as well as the smaller cohort of children at risk (born to hepatitis B+ mothers). The timing of vaccine doses were categorised for each dose into those given on time, missed, delayed by 1 month and delayed by 2 or more months (Delayed ≥2). Table 3 displays the status of the three doses for both sub-populations.
Table 3: Table demonstrating frequencies and percentages of HBV transmission risk (maternal HBV status) and status of vaccinations with TBD, dose 2 and dose 3, in all children and children born to hepatitis B+ mothers (at risk).

<table>
<thead>
<tr>
<th>Variable</th>
<th>All children (n=1928)</th>
<th>Children at risk (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n(%)</td>
<td>n(%)</td>
</tr>
<tr>
<td><strong>Born to Hep B+ Mother</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>99(5.13)</td>
<td>99(100)</td>
</tr>
<tr>
<td>No</td>
<td>1831(94.87)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Missing</td>
<td>33(1.7)</td>
<td>0(0)</td>
</tr>
<tr>
<td><strong>TBD vaccination status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given on time</td>
<td>21(1.1)</td>
<td>4(4)</td>
</tr>
<tr>
<td>Missed</td>
<td>116(6)</td>
<td>5(5.1)</td>
</tr>
<tr>
<td>Delayed by 1 month</td>
<td>497(25.8)</td>
<td>20(20.2)</td>
</tr>
<tr>
<td>Delayed ≥2 months</td>
<td>995(51.6)</td>
<td>58(58.6)</td>
</tr>
<tr>
<td>Missing</td>
<td>299(15.5)</td>
<td>12(12.1)</td>
</tr>
<tr>
<td><strong>Dose 2 vaccination status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given on time</td>
<td>13(0.7)</td>
<td>12(12.1)</td>
</tr>
<tr>
<td>Missed</td>
<td>202(10.5)</td>
<td>11(11.1)</td>
</tr>
<tr>
<td>Delayed by 1 month</td>
<td>333(17.3)</td>
<td>44(44.4)</td>
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<tr>
<td>Delayed ≥2 months</td>
<td>1081(56.1)</td>
<td>19(19.2)</td>
</tr>
<tr>
<td>Missing</td>
<td>299(15.5)</td>
<td>13(13.1)</td>
</tr>
<tr>
<td><strong>Dose 3 vaccination status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given on time</td>
<td>7(0.4)</td>
<td>10(10.1)</td>
</tr>
<tr>
<td>Missed</td>
<td>264(13.7)</td>
<td>14(14.1)</td>
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<tr>
<td>Delayed by 1 month</td>
<td>233(12.1)</td>
<td>31(31.3)</td>
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<tr>
<td>Delayed ≥2 months</td>
<td>1125(58.4)</td>
<td>31(31.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>299(15.5)</td>
<td>13(13.1)</td>
</tr>
</tbody>
</table>
**Descriptive characteristics: Children at risk**

Overall, 99 children were born to 78 hepatitis B+ mothers. Therefore, the proportion of children at risk of hepatitis B was around 5% in this population. Referring to table 3, the percentage of children who received the vaccine doses in this group on time ranged from 4% to 12%. This was the least prevalent type of vaccination status in almost all the groups, with the exception of dose 2, where missed vaccinations were lower. Figures 4 and 5 demonstrates this distribution in frequencies and proportions.

The most prevalent type of vaccination status for all doses consisted of delays (delayed by 1 month & delayed ≥2 months), as demonstrated by the stacked bar graph in figure 5. For the TBD, the most common type of delay was ≥2 months (59%), whilst for the second dose, the largest was 1 month delay (44%) and in the penultimate dose, delays of 1 month and ≥2 months were the same, at 31% each.

The rate of missing doses increased with each progressive dose, from 5% in the TBD, to 11% and 14% in dose 2 and dose 3. This does show however, that 95% of these children received the TBD at some point.

The mean delays for all doses ranged from 2 months in the TBD, and increased to almost 3.5 months in the final 3rd dose (see table 4). For any type of vaccination inadequacy, whether a delay of 1, or ≥2 month delay or missed dose, the TBD had the highest proportion, with a rate of 95%, compared to 86% and 88% in the second and third doses. This is demonstrated in table 5.
Figure 4: Grouped bar graph displaying frequencies of missed dose, given on time and 1 & ≥2 month delays, for the TBD and doses 2 & 3 in children born to HBV+ mothers (children at risk).

Figure 5: Stacked bar graph showing proportions of missed dose, no delay and 1 & ≥2 month delays, for the TBD and doses 2 & 3 in children at risk and All children.
Table 4: Table showing means of dose delays in months with Standard Deviation (SD) for the TBD and doses 2 & 3 in children at risk & All children.

<table>
<thead>
<tr>
<th></th>
<th>TBD mean vaccination delay (months)</th>
<th>Dose 2 mean vaccination delay (months)</th>
<th>Dose 3 mean vaccination delay (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean(SD) Children at Risk</td>
<td>2.04(±1.53)</td>
<td>2.63(±2.02)</td>
<td>3.43(±3.17)</td>
</tr>
<tr>
<td>Mean(SD) All Children</td>
<td>2.23(±2.08)</td>
<td>2.65(±2.49)</td>
<td>3.31(±3.38)</td>
</tr>
</tbody>
</table>

Table 5: Table showing percentage of any inadequacy (missed dose, or 1 or ≥2 month delays) for the TBD and doses 2 & 3 in children at risk & All children.

<table>
<thead>
<tr>
<th></th>
<th>Any TBD inadequacy</th>
<th>Any Dose 2 Inadequacy</th>
<th>Any Dose 3 Inadequacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage (%) Children at Risk</td>
<td>95.40</td>
<td>86.21</td>
<td>88.56</td>
</tr>
<tr>
<td>Percentage (%) All Children</td>
<td>98.71</td>
<td>99.20</td>
<td>99.57</td>
</tr>
</tbody>
</table>

Descriptive characteristics: All Children

The same descriptive analysis on vaccination status was conducted on all 1928 children in the survey, including those who were born to HBV+ mothers. From this group, as displayed in table 3, the proportion of children receiving any dose on time ranged from 0.4% to 1.1%, with dose 3 being the lowest and the TBD being the most covered. Furthermore, vaccinations given on time decreased progressively through each successive dose, from 1.1% to 0.7% to 0.4% in the TBD, second and third doses. These are displayed as proportions and frequencies in figures 5 and 6.

The majority of children across all doses had delayed vaccinations, with the delay of ≥2 months being the most prevalent, each exceeding 50% of vaccination statuses (52%, 56% and 58% in the
TBD, doses 2 and 3). Delays of 1 month decreased in proportion through successive doses, from 26%, to 17% and then to 12% as demonstrated in figure 5. The proportion of ≥2 month delays also changed progressively through the doses, increasing instead. The proportion of missed doses also increases progressively with each successive dose, from 6%, to 11% and finally to 14%.

For the TBD and dose 2, Mean delays in months were higher in this group of children, as displayed in table 4 but was lower in the 3rd dose, still exceeding 3 months. The change in successive doses is summarised in table 5, showing that the percentage of any vaccination inadequacy increased with each dose. The number of missed doses were low in this group, with the majority of children (94%) receiving at least the TBD.

Vaccination data was missing for 13 children in the at-risk cohort, with one child missing data for the latter two doses. For all children in the survey, 299 (16%) had missing vaccination data.

Figure 6: Grouped bar graph displaying frequencies of missed dose, no delay and 1 & ≥2 month delays, for the TBD and doses 2 & 3 in all children.
Associated risk factors for inadequate vaccination

Numerous maternal variables were statistically analysed for association for TBD delay, in order to assess the risk for inadequate vaccination (missed or delayed dose by ≥1 month). Two groups were compared; children who received the TBD on time “TBD adequate” (TBD<1 month) and those who had inadequate TBD vaccination “TBD inadequate” (TBD≥1 month or missed). 21 children were in the TBD adequate group, whilst 1608 children either missed or received a delayed dose in the TBD inadequate group. Frequencies for each reported variable is displayed in table 6, for each group, including resulting p values from statistical analysis.

Maternal HBV positivity

There was a statistically significant association (p=0.02) between maternal HBV status and dose adequacy. Children with adequate TBD vaccination had a higher proportion of HBV+ mothers (almost 20% compared to 5%) compared to the group with inadequate TBD vaccinations. This difference can be observed in figure 7.

Type of place of residence

There was a small difference between the two groups in the type of place of residence, which was not statistically significant. A difference of approximately 5 percentage points was observed, with more mothers living in a rural setting in the adequate TBD group. This is demonstrated in figure 8.

Highest level of education attended

The association between maternal educational level and TBD vaccination was statistically insignificant. The adequately vaccinated group had a higher proportion of mothers who had no education, by almost 10%, whilst both groups had the same proportion mothers who at least attended primary education (76% and 75%). Conversely, the latter group had a higher percentage of children’s mothers who attended secondary education compared to the adequately vaccinated group, with almost a 10% difference, again. Meanwhile, no mothers attended higher education in adequate TBD group, compared to 0.2% in inadequate TBD group. Overall, more mothers attended a higher level of education in the inadequately vaccinated group compared to those
adequately vaccinated. This can be seen in figure 9.

**Maternal literacy**
Overall, a lower level of literacy was observed in the TBD adequate group. There was no statistically significant association, although the difference in distribution in this sample can be observed in figure 10. A higher proportion of mothers had a lower literacy level in the adequately vaccinated group, compared to the inadequately vaccinated TBD group. Over 50% of mothers had the highest literacy level in the inadequately vaccinated group compared to the adequately vaccinated group, by more than 10%.

**Wealth**
There were 5 levels of wealth in the questionnaire, from the poorest to the richest. There was a statistically significant association between wealth and adequacy of TBD vaccination ($p=0.049$). The group of children with inadequate TBD vaccination had more than double the proportion of mothers who had the poorest wealth index (10% vs 24%). However, the same group had no mothers who belonged to the richest wealth index category, compared to 12% in the inadequately vaccinated group.

Overall, the children who had adequate TBD vaccinations had more mothers who were poorer, with 58% below and 23.8% above the middle wealth category, whereas the other group had 47% below and 31% above the middle wealth group. This division can be seen in figure 11.

**Place of delivery, Delivery by C section, Covered by health insurance and HIV positivity**
There were no statistically significant associations between the TBD vaccination status and place of delivery, delivery by c section, covered by health insurance and result of HIV tests. All these variables had at least one cell with 0 responses in the adequate group. Cell counts are displayed in table 6.

The majority of mothers gave birth in public sector for both groups, with more in the adequately vaccinated group, and had not undergone caesarean section (95%). Almost all mothers were not covered by health insurance, with the exception of 1.6% in the inadequately vaccinated group. Finally, the vast majority of mothers were tested negative for HIV in both groups.
Table 6: Table demonstrating frequencies and percentages of various risk factors for children receiving adequate TBD vaccination (“TBD adequate”, <1 month) and inadequate TBD (“TBD Inadequate” ≥1 month or missed), with P values for associative analysis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>TBD adequate N=21 n(%)</th>
<th>TBD Inadequate N=1608 n(%)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Born to Hep B+ Mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4(19)</td>
<td>83(5.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>No</td>
<td>16(76.2)</td>
<td>1499(93.2)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0(0)</td>
<td>26(1.6)</td>
<td></td>
</tr>
<tr>
<td>Type of place of residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>7(33.3)</td>
<td>611(38)</td>
<td>0.822**</td>
</tr>
<tr>
<td>Rural</td>
<td>14(66.7)</td>
<td>997(62)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0(0)</td>
<td>0(0)</td>
<td></td>
</tr>
<tr>
<td>Highest educational level attended</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Education</td>
<td>3(14.3)</td>
<td>86(5.3)</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>16(76.2)</td>
<td>1207(75.1)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>2(9.5)</td>
<td>311(19.3)</td>
<td></td>
</tr>
<tr>
<td>Higher</td>
<td>0(0)</td>
<td>4(0.2)</td>
<td>0.165</td>
</tr>
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<td>Missing</td>
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<td>0(0)</td>
<td></td>
</tr>
<tr>
<td>Literacy</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cannot read at all/ Blind</td>
<td>5(23.8)</td>
<td>319(19.8)</td>
<td></td>
</tr>
<tr>
<td>Able to read only parts of sentence</td>
<td>8(38.1)</td>
<td>468(29.1)</td>
<td></td>
</tr>
<tr>
<td>Able to read whole sentence</td>
<td>8(38.1)</td>
<td>816(50.7)</td>
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<tr>
<td>Missing</td>
<td>0(0)</td>
<td>5(0.3)</td>
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<tr>
<td>Wealth Index</td>
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<td></td>
</tr>
<tr>
<td>Category</td>
<td>Count</td>
<td>Percentage</td>
<td>Value</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>------------</td>
<td>-------</td>
</tr>
<tr>
<td>Poorest</td>
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<td>9.5%</td>
<td>338</td>
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<tr>
<td>Poor</td>
<td>10</td>
<td>47.6%</td>
<td>371</td>
</tr>
<tr>
<td>Middle</td>
<td>4</td>
<td>19%</td>
<td>350</td>
</tr>
<tr>
<td>Richer</td>
<td>5</td>
<td>23.8%</td>
<td>314</td>
</tr>
<tr>
<td>Richest</td>
<td>0</td>
<td>0%</td>
<td>185</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>0%</td>
<td>0</td>
</tr>
</tbody>
</table>

**Place of Delivery**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
<th>Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>4</td>
<td>19%</td>
<td>353</td>
<td></td>
</tr>
<tr>
<td>Public Sector</td>
<td>17</td>
<td>81%</td>
<td>1246</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>0</td>
<td>0%</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Other</td>
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<td>0%</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>0%</td>
<td>3</td>
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</tr>
</tbody>
</table>

**Delivery by Caesarean section**

<table>
<thead>
<tr>
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<th>Percentage</th>
<th>Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1</td>
<td>4.8%</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>95.2%</td>
<td>1533</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>0%</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Covered by Health insurance**

<table>
<thead>
<tr>
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<th>Percentage</th>
<th>Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>0</td>
<td>0%</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>21</td>
<td>100%</td>
<td>1575</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>0%</td>
<td>8</td>
<td></td>
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</tbody>
</table>

**Result of HIV Test**

<table>
<thead>
<tr>
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<th>Percentage</th>
<th>Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>0</td>
<td>0%</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>95.2%</td>
<td>1568</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>4.8%</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

*Fisher’s Exact Test used to derive p value for cell counts <5.*

**Pearson’s Chi-Squared test used instead of Fisher’s exact test, due to cell count >5.*
Figure 7. Stacked bar graph showing proportion of maternal HBV test result status, for children with adequate TBD vs inadequate TBD.

Figure 8. Stacked bar graph showing proportions of maternal type of residence, for children with adequate TBD vs inadequate TBD.
Figure 9. Stacked bar graph showing proportions of maternal highest educational attainment, for children with adequate TBD vs inadequate TBD.

Figure 10. Stacked bar graph showing proportions of maternal literacy, for children with adequate TBD vs inadequate TBD.
Figure 11. Stacked bar graph showing proportions of maternal wealth index, for children with adequate TBD vs inadequate TBD.
Discussion

Key findings & analysis
Descriptive analyses showed a very low vaccination rate given on time, particularly in all the children. Additionally, delays which were over 1 month were prominent in all doses, across both groups. In spite of this, high coverage rates of the TBD were achieved, even though they were severely delayed. Associative analysis demonstrated results that suggest children with a maternal background of the poorest wealth and positive hepatitis B status, and to a lesser extent the lowest education and rural place residence, resulted in a higher chance of the TBD given on time.

Vaccination rates: Children at risk
The results of this study found that dose adequacy was poor, whilst coverage remained high. Few doses were received on time and, concerningly, the TBD had the lowest rate, denoting a poor rate of protection that abides by the WHO’s guidelines. Meanwhile, over half of these children had the TBD delayed for at least 2 months, whilst the proportion of children missing the TBD was higher than those who had it given on time. This is a concerning finding, as without vaccination, HBV is up to 90% likely to cause chronic hepatitis B infection in children born to HBV+ mothers. It was demonstrated in this study that the rate of any vaccination inadequacy for this group, whether the doses were missed or delayed, were persistently high, especially for the TBD. Despite this, the coverage of the TBD was high. This suggests that the policy is effective in vaccination coverage, whereas the quality of vaccination, particularly the timing, remains poor. Overall, the vast majority of children have not had adequate prophylaxis against HBV.

Considering that these children should be protected with stable and consistent health care due to their risk, especially with the most valuable intervention- the TBD, it can be estimated that over 95% of these children may have had less than substantial protection against HBV. The reasons for the poor adherence to the time frame for which the TBD should be administered are multifactorial, involving many factors, including policy. The findings of the associative analysis are discussed further in this section.
Vaccination rates: All children

The vaccination adequacy of the general population of children, regardless of maternal infection status, was poor. The rate of TBD vaccinations given in all children of this study, regardless of transmission risk, was 1%. Most children received the doses late, denoting a greatly reduced rate of hepatitis B protection, as the prophylactic efficacy of the TBD is reduced with greater delays. With successive doses, vaccinations given on time suffered from a progressively lower rate. This may be due to a number of reasons, such as children being lost to follow up, moving residence or parents not seeing the point of vaccinating further.

Overall, almost all children in this survey suffered from some form of dose inadequacy. Therefore it can be suggested that almost all of the children in this survey have not received adequate prophylaxis against HBV, thus negating the efforts in having a universal TBD policy since timing is crucial. It can be said therefore, that although the influence of the TBD policy has had a positive effect on children being vaccinated against HBV to obtain at least some protection, the efficacy of the vaccine is undermined by its poorly timed implementation, which the policy seems to have lacked influence over.

If the results of both groups are compared, it can be seen that the proportion of children who received any vaccination on time, was higher in the group of children at risk than the whole population of children generally. This may be because the maternal HBV positivity status may have already been known to healthcare professionals, and these children were thus subjected to extra care, and hence a higher rate of coverage. Universally however, the TBD must be given within the correct timeframe for prophylaxis to be effective for the whole population, and thus, the reduction in transmission risk. Although the aim of this study was not to compare the results of both these populations, as the second group included the first, this analysis has shed light on the increased risk of those born to infected mothers in the context of the general population.

Universal TBD coverage is recommended for settings with moderate to high prevalence, as a strategy to protect against HBV MTCT. Selective screening of high risk pregnant women, whilst being the key strategy in low prevalence countries with established robust healthcare systems, is
less feasible in a lower income setting, with limited time and resources. Thus, the TBD is an important component of the general vaccination schedule for children in these countries, and is best given at the point of birth to all children.

**Comparison amongst literature: Vaccination adequacy & TBD policy**

This analysis demonstrated a low coverage of the TBD in not just the general population of children, but those at risk, within the surveyed participants. In Nigeria, another lower middle income country in SSA, a TBD policy was also introduced a year before São Tomé and Príncipe, in 2004. Nigeria is also geographically close to São Tomé and Príncipe, with only a body of sea separating the two countries. A hospital based study conducted in 2014 observed an adequate HBV immunity rate of 83% amongst 148 children, but with a mean age of 28 days (SD: ±20.4) for the administration of the TBD. Completion of the vaccination schedule was a mean of 110 days (SD±18.6), just under four months after birth. Despite the high level of HBV vaccination coverage, seroprevalence, the detection of the HBV in blood, was found to be almost 14%. This likely meant that 14% of infants had acquired the infection via MTCT, despite vaccination. Whilst it is difficult to compare the adequate immunity rate of the children in the present study since HBV seroprotection tests were not conducted in the survey, 84-93% of children received the 3 doses, which suggests similar immunity rates. Additionally, the mean time of vaccination for the TBD was 2 months and, over half the children similarly received dose 3 around four months after birth. The study shows similar trends of generally high vaccination rates, but poor adequacy of timing in all doses. There is a difference in study periods however between the two studies, with seven years difference, and the results measuring changes 10 years after the implementation of national guidelines in Nigeria, compared to 3 years after implementation, in this study. Another aspect to consider when comparing these two studies is the inclusion of children ages 2-15 years in the Nigeria study, which differs from the survey data collected in the DHS questionnaire, ranging from ages 0-5 years.

The Gambia is a low income country also on the west coast of SSA, which saw the introduction of the TBD prior to the turn of the century. Recently, a study was conducted there in 2016 using a demographic health survey (FHDSS), analysing TBD vaccination as well as associated
barriers. In the study, a majority of children received the TBD, and in fact the rate was the same as the present study (93%). Interestingly, the rate of TBD given on time was the same as the rate observed in this study (1.1%), whilst the study also found that a majority of these were delayed by at least a month (58% by day 28). Important to note, is that the findings in this study is a reflection of the state of TBD adequacy many years after implementation of a policy. Thus, it may be assumed that although the DHS survey in São Tomé and Príncipe was conducted only a short period of time after the implementation of guidelines, little may change its effect, thus coverage rates and similarly adequacy of these vaccinations may change slowly with time.

To summarise the findings in these two studies and compare with the findings of this research, national TBD guidelines are effective in achieving a high coverage rate of HBV vaccination, however difficulties still persist in adequately vaccinating children in a timely manner, particularly with the TBD. Additionally, with The Gambia being a low income country, the findings of this paper suggest that the vaccination practices within São Tomé and Príncipe are more akin to a low income setting, rather than a lower-middle income setting, such as Nigeria. This is evidenced by a higher rate of delays at one month (26% after first month, 52% after second month in this study) whereas 58% received the TBD within a month in the Gambia.

The purpose of a universal TBD policy is for prophylactic protection against HBV transmission, in the event that a child is born to an infected mother. In the USA, a high income country, implementations of TBD policies are variable and depend on local guidelines, rather than national ones. One cross sectional survey study in the USA of 4786 infants found that 67% of infants at risk received a TBD whilst 13% had not, by the time of discharge. Although the rate of adequate TBD was high compared to this study in São Tomé and Príncipe, it still demonstrated that almost one third of children born at risk were not adequately protected, in this high income setting. Additionally, a lower rate of 52% of children born to mothers of unknown HBV status received the TBD adequately, whilst 20% did not receive the TBD before discharge. These findings demonstrate the influence of pre-emptive knowledge on the successful administration of the TBD.

Similarly in Canada, another high income country in North America, a retrospective study
reviewed the public health records of 725 infant-mother pairs at risk of MTCT of HBV. This time, 80% of children born to HBV+ mothers received the TBD correctly, whilst the rest did not\textsuperscript{47}. Thus in comparison to the present study, the TBD coverage rate of any such TBD was high. As demonstrated by this study therefore, the difference between a resource rich setting and a lower resource one, such as São Tomé and Príncipe, is vast.

Risk factors
Associative analysis for risk factors previously identified yielded mixed results. Maternal HBV positivity and low wealth was significantly associated with increased TBD adequacy, whilst other factors suggested influences on vaccination adequacy. These findings however were plighted by a small sample size.

Maternal HBV positivity and Wealth
A statistically significant association was found when examining the HBV positivity in mothers. A greater proportion of children born at risk had received the TBD on time. This confirms the observed trends previously discussed, where children who were adequately vaccinated, were more likely to have been from a Hep B+ mother. It can be deduced therefore, that if there was no perceived risk to the child from an infected mother, the TBD was less likely to be given adequately, on time.

It is not known if there was screening during the antenatal period for maternal HBV status, or whether women from high risk backgrounds were screened prior to birth in São Tomé and Príncipe. However these findings suggest some form of pre-emptive knowledge of HBV status, resulting in higher rates and quality of vaccination. In addition, although this preceding knowledge has influenced child vaccinations positively, correctly performed universal vaccination can ensure the same outcome, if not better, with considerably less effort and cost compared to comprehensive screening as the major strategy against HBV, particularly in this lower-middle income setting.

The association between maternal wealth of the child and TBD adequacy was found to be statistically significant. Children who were adequately vaccinated with the TBD were from a
generally poorer background. Families subjected to poverty may have limited resources and access to healthcare, thus it may seem paradoxical that such an association is made. Lower status of wealth is noted as a risk factor for poor vaccination\textsuperscript{15}, however it is also known that those from a poorer background may be subjected to a higher risk of hepatitis B prevalence\textsuperscript{48}. Knowing this, and that HBV+ mothers received better coverage of adequate TBD vaccination, it can be assumed that more of these women from poorer backgrounds were known to be HBV+, and thus received a higher rate of adequate TBD. Again, the screening methods for mothers, particularly targeting of high-risk women is not known for this setting, but this strategy may have played a part at the health provider level.

\textit{Maternal place of residence, educational level and literacy}

It has been noted in other research in similar settings\textsuperscript{16-20}, that a rural setting may denote a lower chance of successfully receiving the TBD for children. This is due to transportational, logistical as well as birth notification issues. The contrary was suggested in the present study, where there were fewer children who were inadequately vaccinated in a rural place of residence, compared to those who were vaccinated adequately, although this was not a statistically significant finding. This finding may be the result of a higher proportion of poorer mothers, and thus a higher prevalence of hepatitis B, leading to better TBD coverage, since lower socioeconomical status and rural place of residence is linked.

In the study conducted in The Gambia assessing TBD coverage, risk factors for barriers to the TBD was also collected. The study found that individuals living in a rural setting were also significantly more likely to receive the TBD within 7 days than those in an urban setting. This was attributed to village based primary health care services in The Gambia\textsuperscript{45}. Since the details of São Tomé and Príncipe’s primary health care system is unknown, it is not certain whether this was also the reason for the association found in this study.

There was a non-statistically significant higher level of education seen in the inadequately vaccinated group, compared to those who were vaccinated adequately. Maternal knowledge and understanding is thought to increase the rate of coverage of HBV vaccination\textsuperscript{28}. In the Gambian
study\textsuperscript{45}, maternal education was significantly associated with higher vaccine coverage at 7 days. The contrary is demonstrated in the present study; however this may also be linked back to low socioeconomical status thus poorer education, and higher maternal HBV prevalence, resulting in increased TBD coverage.

A higher literacy level was seen in the inadequately vaccinated TBD group; however this association was also not statistically significant. In other studies, a low level of maternal literacy is suggested to result in lower coverage rates for TBD administration. Mothers with low literacy levels are less able to access information and better healthcare; however this may be more relevant in higher income settings, due to the higher numbers of migrant mothers. In this study, the low literacy level of mothers whose children had adequate TBD vaccination may be again, linked back to poverty, and thus a higher proportion of HBV+ mothers.

*Maternal place of delivery, delivery by caesarean section, covered by health insurance and HIV testing*

The following variables had P values of >0.99, suggesting statistically insignificant results. The quality of statistical analysis however, may be attributed to some cell counts having just one response and or none.

The place of delivery has been suggested to have some influence on successful TBD coverage rates in previous studies. Public sector births tend to have better TBD coverage than home and private sector births, due to organised and prioritised vaccination services\textsuperscript{20,23}. In this study, births in the public sector had a slightly higher proportion of children with adequate TBD vaccination. The Gambian study also found no significant results regarding vaccination timeliness and place of birth\textsuperscript{45}. This suggests that in the SSA setting, the influence of healthcare facilities is not as important as it is in other contexts, such as those in Asia. With a geographical context that is fragmented by its island setting, this finding is somewhat surprising.

There was little difference in the aspects of maternal caesarean section, health insurance coverage and HIV testing when comparing TBD adequacy in this study. These suggested risk
factors have little presence in this setting, given that caesarean section and health insurance are factors important in middle to high income countries. The % prevalence of HIV amongst adults in São Tomé and Príncipe was less than 1% in 2012\(^{49}\), comparatively less in Nigeria, which was 3.1%\(^{50}\). Thus the numbers obtained in the subpopulations for this analysis were not enough for any significant findings.

Overall, it is clear that the risk factors included for analysis, as depicted in the conceptual map in figure 1, were less indicative of TBD adequacy as initially hypothesised. These variables were chosen according to availability of variables within the survey, but more importantly, guided by the body of research regarding the subject around the world. Of note, due to the paucity of data from SSA, the majority of these were from a different context.

**Strengths and limitations**

Since 2005, São Tomé and Príncipe have introduced the TBD, but national policy is only one piece of the puzzle. Due to the limits of the data collected within the DHS survey, no data regarding the HBV status of the children were available, thereby limiting this study to a simple observational analysis. In order to ascertain the effect of the national immunisation programme of São Tomé and Príncipe, child HBV status data would have allowed for a more in-depth risk analysis such as prevalence estimates for children at high risk of transmission and those in the general population.

Despite this, by using data on maternal HBV status, this study was able to give an estimate of the proportion of children who were at risk of transmission and their varying levels of TBD vaccination adequacy. This analysis was also stratified for their peers.

The DHS-V survey used as secondary data for this study took place between 2008-2009. This survey type omitted the inclusion of the full date of birth for children, which was included in the following survey iteration, DHS-VI. Thus, this study was only able to calculate the timing of doses based on months and years only.

The lack of a day of birth variable therefore was a major limitation to the accuracy of the categorisations and interpretation of TBD adequacy. Lack of this variable affected the
categorisation of dose timings, and neglected the dimension of magnitude with regards to delays. For instance, a delay of 31 days would have held the same category (delayed by 1 month) as a delay of 59 days. Overall, by the WHO’s standards, the findings of this study would give little indication of the study sample’s adherence to the strict rule of TBD given within 24 hours. However, as observed in the results, very few of the sample achieved adequate TBD vaccination within a month. Given the wider perspective of large delays and distribution within this sample, broader categorisation using the WHO’s AFRO guidelines (within a month) has been deemed appropriate for this setting. This itself is a notable finding, that very few infants achieved even the 1 month time limit, revealing a public health issue that needs to be addressed. Additionally, if the categorisation of delays included a definition of within 24 hours, the subpopulation of adequate TBD would have been even smaller, limiting the value of statistical tests. Furthermore, the results of this study reflects the early stages of the policy’s implementation, thus analysis using more accurate data would perhaps be better suited once the policy has matured sufficiently.

The same issue persisted for the second and third doses, however the impact of the magnitude of the delay, is less here. The interpretation of the results of this study should therefore be approached with this in mind, and that the status of “given on time” might not necessarily comply with the WHO’s official guidelines for TBD, but is valid for the AFRO regions WHO guidelines
text

The variables used for this study mainly revolved around the maternal aspects that may influence the effectiveness of TBD administration. This left little scope for other factors, such as those concerning healthcare facilities, environmental and cultural aspects. Certain variables such as Prenatal Doctor (presence of doctor during prenatal care) were only collected for the last child born, thus they were excluded. Additionally, sociodemographic factors were not included into the associative analysis of the study, thereby limiting the scope of analysis. This study was also limited through the omission of girls and women above and below the surveyed age limits of 15-49 years old. The exclusion of these individuals limits the representativeness of this study, as the children born to girls and women outside this range are not included into the descriptive and risk analysis. This is also perhaps an important factor that neglects the issue of early adolescent pregnancy, another global health issue that is in need of
further research.

Another limitation to this study, or rather the discussion of it, is the paucity of other surveys with data on HBV prevalence and vaccination. Since there are no other DHS surveys on this topic, no comparison can be made with this study. To impound this problem, a DHS survey conducted in São Tomé and Príncipe in 2015-16 did not collect these data on HBV status. Frustratingly, the recent DHS survey also collected more accurate DOB data, including the date of birth. These factors restricts any future study using similar methods and data for a more accurate comparison.

**Internal validity**

*Vaccinated children before 2005*

The DHS-V survey collected child vaccination data for children born up to 5 years prior to the survey, meaning that the vaccination dates of children born from 2003 was included. Since the TBD policy was introduced in 2005, a proportion of children may have been vaccinated according to the guidelines prior to the policy change, which is not known. Thus, the findings of this study pertaining to the effectiveness of the TBD policy may have been affected by children vaccinated before this time, without an emphasis on the TBD. Due to the low number of participants with vaccinations given on time in this study, these children prior to 2005 were kept for analysis, however, analysis excluding these children may well have yielded more positive results regarding TBD vaccination status.

*Maternal HBV testing*

Another limitation related to the secondary data was the reported maternal HBV blood test results, which was obtained during the survey. The result is a reflection of the HBV status of the individual at the time, therefore it is unknown whether the mother was infected with HBV before or after the birth of her child/children. This makes it difficult to say accurately whether true MTCT was a risk for the group of children “at high risk”. It is therefore important to assess these results with this in mind; however whether the mother’s HBV status was acquired before or after the birth of her children, adequate TBD vaccination is still required in these children especially, since horizontal transmission through interpersonal contact is a possible route of transmission.
Small subpopulations

Very few children received any dose on time, thus reducing the size of the subpopulations analysed. This was not a limitation or problem of the secondary data itself, rather a problem at the sample-population level. This very finding may be highlighted as an issue of the efficacy of the policy, as well as being a limitation to the analysis of the data itself, within this study. Although the smaller sample size affects the sensitivity of the statistical tests performed in the associative analytical aspect of this study, as a descriptive finding, this is revealing of the state of hepatitis B vaccinations in the survey population, and potentially, the nation of São Tomé and Príncipe itself.

Confounding analysis

The problem or finding, depending on how one views it, of small subpopulations, impacted on the ability of this study to conduct confounding analysis. Multivariate regression or other statistical methods were not utilised as larger sample sizes are required for these. One solution considered, was to include those who had a delay of 1 month into the group of adequately vaccinated, however due to the nature of the secondary research question; to analyse the TBD adequacy according to various factors, this would have been a substantial deviation from the initial research aim. Thus, the lack of confounding adjustment must be considered in the interpretation of these findings, and these results may give a raw estimation of the factors at play in this study area.

Generalisability & relevance

Study context: São Tomé and Príncipe

Around the world, the TBD has been introduced through national policy in order to reduce the transmission of HBV. Out of 195 countries, 70 various low, middle and higher income countries have implemented this policy, with only 7 countries in SSA contexts including São Tomé and Príncipe. It is important for the public health field to gain knowledge and understanding of the effectiveness and implementation of this policy, in addition to factors outside of the national policy which may affect it. The understanding of social, cultural and environmental factors
outside the domain of policy is key in improving and targeting its implementation in order to boost its efficacy and coverage.

The nation of São Tomé and Príncipe is unique in its context within SSA, due to its small island setting. From an interpretive point of view, the findings of this study should consider the small size and coastal environment into account when applying them to different contexts. A much larger SSA country may have vast areas of land uncovered by healthcare facilities or community health outreach services, and varying terrains through which either healthcare professionals or pregnant women must travel for birth. Additionally, cultural and societal aspects are varied in the African continent, from the antenatal, perinatal and postpartal periods of motherhood. Furthermore, due to the coastal-island setting, the islands of São Tomé and Príncipe may suffer from a fragmented health system due to the physical distance and body of sea between the two islands and its smaller pieces of land in the archipelago. Despite the centralised effort of instilling national guidelines, distribution and practices throughout the nation may suffer from inconsistent and varying levels of implementation, not to mention discrepancies in the levels of healthcare delivery. It is also worth noting that the introduction of TBD policy was implemented three years prior to the start of survey, thus it may be difficult to attribute the effect of this in a short period of time.

An aspect that was mentioned previously, was the sample population. The sample population was limited in the included age ranges for the survey. Nevertheless, this study analyses the TBD coverage and affecting factors in a lower-middle income setting, and readers of the study may appreciate the same limiting factors that similar settings share.

**HBV vaccination: Evidence and challenges in Public Health**

In order to achieve the WHO’s Global Health Sector Strategy on Viral Hepatitis 2016-2030\(^1\); to eliminate viral hepatitis as a global public health concern, an understanding of the factors contributing to MTCT is vital. This is in addition to the challenges to the proper implementation to key strategies, such as the Timely Birth Dose.

The comparability to other research has been discussed thus far, and it has been clear that the
body of evidence agrees with the findings in this study in some areas, such as the high coverage rate but low adequacy of vaccination despite policies, as well as certain risk factors. It has shown the severe challenges facing SSA countries in giving vaccinations on time, but more research is required in order to understand the context of these environments, as well as the factors outside of policy that may play a role. There yet remains a large proportion of populations that may benefit from adequate TBD administration and until this need is addressed, the few TBD policies that exist in the SSA context may fail to achieve true universal HBV protection. Thus, although incorporating the TBD policy is a first step, much more work is needed in the public health field, in order to reduce the morbidity and mortality caused by HBV, as shown in this study, and others.

Indeed there remains the research priority of understanding risk factors and barriers to this implementation also. These studies taken together have highlighted however, the socio-economical inequities of vaccination practices amongst those of different levels of wealth and to a lesser extent education, literacy and place of residence. Perhaps therefore, an angle of empowerment of mothers and healthcare providers should be targets for tackling these inequalities, future research and innovation in the SSA context.

**Conclusion**
This study has shown that although the coverage of vaccinations was high, only a small proportion of children received doses on time, including children at high risk of transmission. This suggests that the TBD policy ensures a higher rate of vaccination, however the impact on the quality, namely timing, remains poor. Associative analysis showed that socioeconomic factors such as pre-existing HBV infection and wealth are interconnected, and confers a higher rate of adequate TBD vaccination. This shows a discrepancy in TBD vaccination between women of different socioeconomical statuses. Other risk factors reviewed in this study suggested this link, however statistical analysis was ultimately inconclusive, namely due to poor vaccination quality amongst the study population. To understand and deepen the knowledge in this field, more in-depth studies may be required, particularly of qualitative design, which is outside the scope of this secondary analysis. Other more holistic methods may need to be employed in order to further or supplement the TBD policy in São Tomé and Príncipe, with an
emphasis on addressing the inequalities and empowerment of potential mothers.
The timely birth dose is a simple, but effective tool capable of battling the burden of HBV in low-resource settings, however there yet remains a rift between its utilisation in policy and proper utilisation in the field.

References


32. WHO, UNICEF. *IMMUNIZATION SUMMARY: A statistical reference containing data*


34. USAID. SURVEY ORGANIZATION MANUAL FOR DEMOGRAPHIC AND HEALTH SURVEYS. Calverton: ICF International; 2012.


40. Instituto Nacional de Estatística - INE/São Tomé e Príncipe, Ministério da Saúde, and
http://www.dhsprogram.com/publications/publication-FR233-DHS-Final-Reports.cfm#sthash.RNps3Kgm.dpuf

41. USAID. Survey Summary: São Tomé and Príncipe: Standard DHS, 2008-09.  


Http://www.who.int/wer/2009/wer8440.pdf?ua=1


49. Unicef. *At a glance: Sao Tome and Principe*. 

50. Unicef. *At a glance: Nigeria*. 

**Annex**

**Table 1:** Table showing questionnaire code, name, labels (with comments) and missing responses (%), for variables used in study.

<table>
<thead>
<tr>
<th>Code</th>
<th>Variable 1</th>
<th>Label/ Comments</th>
<th>Missing (NA) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>v025</td>
<td>Type of place of residence</td>
<td>1: Urban, 2: Rural</td>
<td>0</td>
</tr>
<tr>
<td>v106</td>
<td>Highest educational level attended</td>
<td>0: No education, 1: Primary, 2: Secondary, 3: Higher, 9: Missing</td>
<td>0</td>
</tr>
<tr>
<td>V155</td>
<td>Literacy</td>
<td>1: Cannot read at all/ Blind/ Visually impaired, 2: Able to read only parts of sentence, 3 Able to read whole sentence</td>
<td>8/2623(0.31)</td>
</tr>
<tr>
<td>V190</td>
<td>Wealth Index</td>
<td>1: Poorest, 2: Poorer, 3: Middle, 4: Richer, 5: Richest</td>
<td>0</td>
</tr>
<tr>
<td>B301</td>
<td>DOB Child 1</td>
<td>mm/yy</td>
<td>0</td>
</tr>
<tr>
<td>B302</td>
<td>DOB Child 2</td>
<td>mm/yy</td>
<td>0</td>
</tr>
<tr>
<td>B303</td>
<td>DOB Child 3</td>
<td>mm/yy</td>
<td>0</td>
</tr>
<tr>
<td>M151</td>
<td>Place of Delivery(child 1)</td>
<td>10: Homes, 20: Public sector, 30: Private Sector, 96: Other</td>
<td>9/1445(0.62)</td>
</tr>
<tr>
<td>-------</td>
<td>---------------------------</td>
<td>------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>M152</td>
<td>Place of Delivery(child 2)</td>
<td>10: Homes, 20: Public sector, 30: Private Sector, 96: Other</td>
<td>19/448(4.24)</td>
</tr>
<tr>
<td>M153</td>
<td>Place of Delivery(child 3)</td>
<td>10: Homes, 20: Public sector, 30: Private Sector, 96: Other</td>
<td>4/37(10.81)</td>
</tr>
<tr>
<td>M171</td>
<td>Delivery by caesarian section (child 1)</td>
<td>0: No, 1: Yes</td>
<td>2/1445(0.14)</td>
</tr>
<tr>
<td>M172</td>
<td>Delivery by caesarian section (child 2)</td>
<td>0: No, 1: Yes</td>
<td>1/448(0.22)</td>
</tr>
<tr>
<td>M173</td>
<td>Delivery by caesarian section (child 3)</td>
<td>0: No, 1: Yes</td>
<td>0</td>
</tr>
<tr>
<td>V481</td>
<td>Covered by Health insurance</td>
<td>0: No, 1: Yes</td>
<td>10/2615(0.38)</td>
</tr>
<tr>
<td>HIV1</td>
<td>Result of HIV Test</td>
<td>0: No, 1: Yes</td>
<td>65/2615 (2.49)</td>
</tr>
<tr>
<td>Variable (Code)</td>
<td>Description</td>
<td>Value</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>S528AH</td>
<td>Result of hepatitis B test</td>
<td>1: Positive, 2: Negative, 3: Indeterminate (recoded as missing)</td>
<td>63/2165(2.91)</td>
</tr>
<tr>
<td>s5061</td>
<td>Hepatitis vaccination- last child</td>
<td>0: Not given, 44: Marked on card, 66: Mother reported, 97: Inconsistent, 98: Don’t know</td>
<td>182/1445(12.60)</td>
</tr>
<tr>
<td>s5062</td>
<td>Hepatitis vaccination- second last child</td>
<td>0: Not given, 44: Marked on card, 66: Mother reported, 97: Inconsistent, 98: Don’t know</td>
<td>94/448(20.98)</td>
</tr>
<tr>
<td>S5063</td>
<td>Hepatitis vaccination- third last child</td>
<td>0: Not given, 44: Marked on card, 66: Mother reported, 97: Inconsistent, 98: Don’t know</td>
<td>14/37(37.84)</td>
</tr>
<tr>
<td>Delay1C1-3</td>
<td>Delay dose 1 Child 1-3</td>
<td>mm- (number of months)</td>
<td>182/1445(12.60) (overall 15.03)</td>
</tr>
<tr>
<td>Delay2C1-3</td>
<td>Delay dose 2 Child 1-3</td>
<td>mm- (number of months)</td>
<td>94/448(20.98)</td>
</tr>
<tr>
<td>Delay3C1-3</td>
<td>Delay dose 3 Child 1-3</td>
<td>mm- (number of months)</td>
<td>14/37(37.84)</td>
</tr>
</tbody>
</table>

Table 2: Table showing Variable name (Code) as described in questionnaire, as well as description, from the Demographic health survey recode manual. Variable recodes and notes also included.
<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest educational level attended(v106)</td>
<td>was interviewed, based on cluster/ sample point classification, as rural or urban. Standardised variable categorising different levels of women's education.</td>
</tr>
<tr>
<td>Literacy(V155)</td>
<td>Whether women who attended primary school can read a sentence. Merged categories Cannot read at all/ Blind/ Visually impaired.</td>
</tr>
<tr>
<td>Wealth Index(V190)</td>
<td>5 point index indicating wealth. Culminates household living standards using indicators such as ownership of assets, televisions, housing construction and water and sanitation.</td>
</tr>
<tr>
<td>DOB Child 1,2 &amp; 3(B301-3)</td>
<td>Child’s month and year of birth (mmyy) calculated from Month of birth(B1), Year of Birth(B2) variables.</td>
</tr>
<tr>
<td>Place of Delivery(M15)</td>
<td>Location of delivery for child. Merged and recoded from the following variables - 10: Homes, (Respondents’ Home, 12: Other home), 20: Public sector (Govt. hospital, Govt health Centre, Health Post, Community Field Worker, Other Public, 30: Private Sector (Private Hosp/ Clinic, Private Nurse, Other Private Medical) 96: Other.</td>
</tr>
<tr>
<td>Delivery by caesarian section(M17)</td>
<td>Whether child was born via caesarian section.</td>
</tr>
<tr>
<td>Covered by Health insurance(V481)</td>
<td>Whether the respondent is covered by any health insurance.</td>
</tr>
<tr>
<td><strong>Result of HIV Test(HIV1)</strong></td>
<td>Result of HIV blood test. Merged from HIV Dataset with matched cases into primary dataset</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Result of hepatitis B test(S528AHH)</strong></td>
<td>Result of Hepatitis B blood test</td>
</tr>
<tr>
<td><strong>Hepatitis vaccination- last 3 children(s5061A-C)</strong></td>
<td>Date of vaccination of last 3 children within 5 years. mmyy format - Recoded date variable from S506m,y column 1,2 &amp;3</td>
</tr>
<tr>
<td><strong>Delay dose 1 Child 1-3(Delay1C1-3)</strong></td>
<td>Delay in Hep B vaccination from the date of birth, expressed in months. Calculated by taking difference of Hepatitis Vaccination date(S5061) from computed DOB(B301-3)</td>
</tr>
<tr>
<td><strong>Delay dose 2 Child 1-3(Delay2C1-3)</strong></td>
<td>Delay in Hep B vaccination from the date of birth, expressed in months. Calculated by taking difference of Hepatitis Vaccination date(S5062) from computed DOB(B301-3)</td>
</tr>
<tr>
<td><strong>Delay dose 3 Child 1-3(Delay3C1-3)</strong></td>
<td>Delay in Hep B vaccination from the date of birth, expressed in months. Calculated by taking difference of Hepatitis Vaccination date(S5063) from computed DOB(B301-3)</td>
</tr>
</tbody>
</table>