Dynamic Modelling of HBV MTCT with an Intervention at the Time of Birth.

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1 How the Literature is Informing the Modelling Process

The paper [Pan et al., 2012] did a review of articles published between 1975-2011 on HBV mother-to-child transmission and deduced that by administering Hb immunoglobulin alongside the Hb vaccine between the time of birth and at most 12 hours after exposure, combined with administering the existing vaccination regimen between 6-12 months to an infant provides an approximate 95% chance of preventing perinatal transmission of HBV from an HBsAg-positive pregnant woman to that infant. The paper also asserted that administering Hb immunoglobulin not long before birth and giving the infant the two doses of Hb vaccine, or avoiding breastfeeding had no impact on HBV MTCT. Furthermore, the authors stated that an efficient way to prevent MTCT of HBV is to assess the risk of MTCT, and to identify the mothers who possessed the most risk so as to administer the interventions to prevent MTCT. Eventually, they listed: maternal level of HBV DNA $> 200,000$ IU/mL, positive test(s) for the HB envelope Antigen(HBeAg) and HB surface Antigen(HBsAg), pregnancy complications such as threatened pretem labour, or prolonged labour, and failure of the immunoprophylaxis in children who had received it, as the risk factors to consider.

2 Suggested Interventions to be Applied to the Neonates

The following interventions have been suggested:

1. Administering at least, a single dose of HB immunoglobulin(HBIg) to the neonates within 12 hours after delivery in addition to the HB vaccine. A delay in the suggested could lead to vertical transmission if the neonate is HB-negative but born to an HB-positive mother, or pre-exposed to the infection[Pan et al., 2012]. HBIg given alongside the HB vaccine at birth provides a stronger protection than administering either interventions alone [Pan et al., 2012].

3 Assumptions of the Model

1. Infants below one year do not die of hepatitis b related causes.
2. The vaccines are not 100% efficient for all individuals.
3. The possibility of horizontal infection in adults.
4. No antepartal interventions for preventing MTCT are put in place.
5. Full protection is possible, and is acquired in one of two categories:

- infants who get a first dose at birth in addition to the current vaccine regimen, and
- other uninfected individuals who get vaccinated.

4 Model Considerations

Since the timing of vaccination is important, individual ages at the time of vaccination were split into:

- newborns at most a day old and herein labelled as $b1$,
- neonates older than 1 day and at most, a year old, herein labelled as $b2$, and
- pregnant mothers, labelled as m herein, who grew from the previous age category.

5 Model Framework

The model flowchart was generated by linking up three interacting models of two types: $SVVPIT$ for neonates of age-class $b1$, and $SVPIT$ for infants of age-class $b2$ and pregnant adult females of category m.
The model consists of the following class of individuals: susceptible individuals (S_m), (S_{b1}) and (S_{b2}), infants who have received their first dose at birth or within 24 hours (V_{b1}), and infants who have received their full dosage of the current vaccine regimen (V_{b2}). It is worth noting that the class V_{b2} contains neonates who were vaccinated at birth and those who were not, so far as they remained uninfected. The other classes are: fully protected individuals (P), infected individuals (I), a class of individuals who have been treated, or are under treatment (T).

5.1 Flowchart Description

Neonates are either born infected or uninfected and that is how S_{b1} and I_{b_1} are populated. Some of these individuals receive their first dose immediately after birth, moving to V_{b1}. Since it is assumed the first dose does not provide full protection, some of the vaccinated neonates may be infected before they receive the second set of vaccines; those individuals populate I_{b1} alongside those infants who get infected because they were not vaccinated. Since the vaccine may wane off, some of the vaccinated individuals in V_{b1} may become susceptible to infection and move back into class S_{b1}. The non-vaccinated (and uninfected) neonates of age less than one day will flow into the S_{b2} class where they may be vaccinated and proceed to the V_{b2}. As a result of being uninfected from birth, and having developed a stronger immune system, we assume they will acquire full protection thereof, and flow into the class P. The infants who were both administered the first dose and the current regimen will be recruited into P too. The vaccine-based immunity may wane off; those individuals will again become susceptible hence, returning to S_{b2}.The class P will serve as a sort of reservoir for keeping track of individuals who have been eliminated from the infection cycle. Some of the individuals in classes I_{b1} and I_{b2} may be put under treatment and that is how individuals in classes T_{b1} and T_{b2} will be recruited. Susceptible pregnant women are recruited from the proportion of susceptible female infants who escape both vertical and horizontal transmission. All infected infants remain infected, some of whom become pregnant and move into I_m. The treated individuals who remain under a lifetime treatment and become pregnant will populate T_m. Some of the susceptible pregnant women will eventually be vaccinated, and assuming they will become fully protected as a result, they will move to class P. Those who lose their vaccine-induced immunity may become infected and move to class I_m or remain susceptible and hence move back to class S_m. In all classes, individuals may be

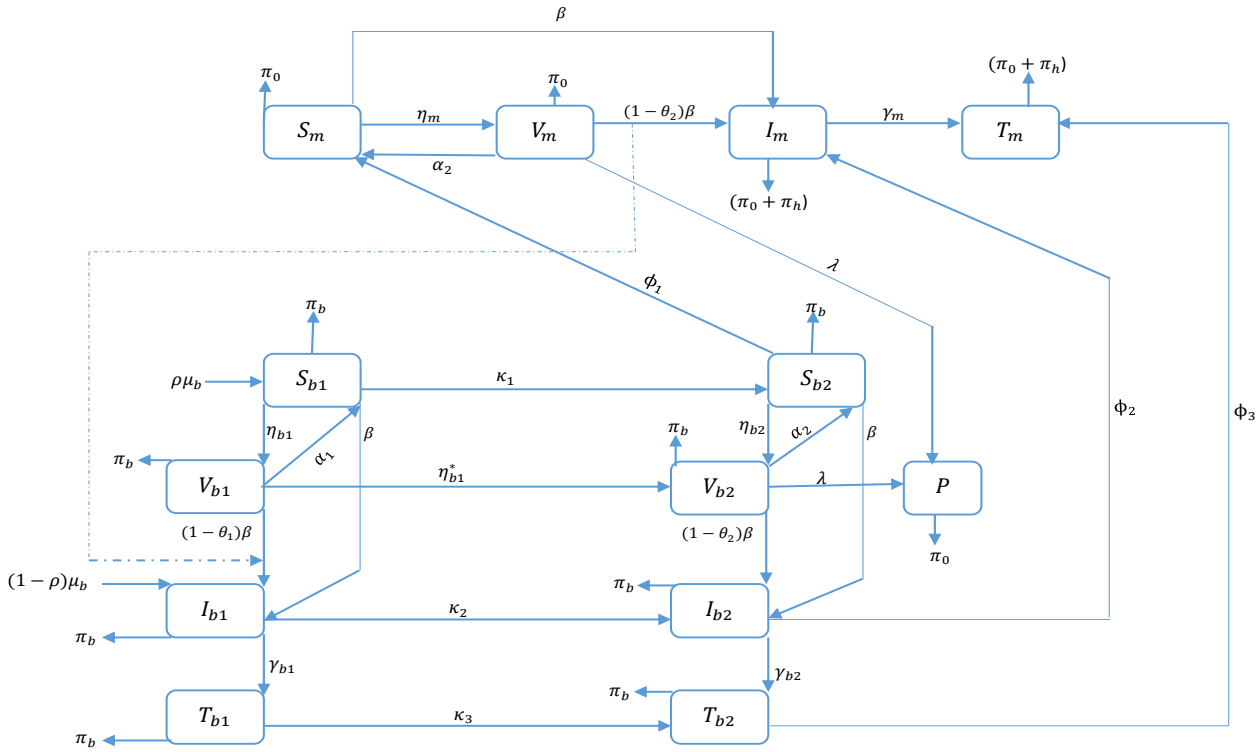

Figure 1: Model Flowchart

removed by natural death, HBV-related mortality, or for the infants, by some infant-mortality-related causes.

The flow chart is represented in Figure 1. The equations will be generated subsequently upon discussing the flow diagram and after all necessary inputs have been implemented and approved.

5.2 Description of Parameters

The following are the variables and parameters used so far:

S_{b1}: Susceptible neonates below age 1 day

S_{b2}: Susceptible neonates older than age 1 day without a first dose at birth

S_m: Susceptible pregnant women

V_{b1}: Vaccinated neonates at time of birth

V_{b2}: Vaccinated infants with or without a first dose at birth but of the age-class $b2$

V_m: Vaccinated pregnant mothers

P : Protected individuals (refer to assumptions for details)

V_m: Vaccinated pregnant women

I_{b1}: Infected neonates below 1 day old

I_{b2}: Infected neonates older than 1 day but at most, a year old.

I_m: Infected pregnant women

T_{b1}: Neonates below age 1 day and are under treatment

T_{b2}: Infants older than 1 day old, but at most, a year old, and under treatment

T_m: Pregnant women under treatment.

π_0: Natural death rate (assumed to be the same across ages)

π_b: Infant mortality rate

π_h: hepatitis b related death rate

μ_b: Birth rate

ρ: Proportion born uninfected

ϕ_1: Proportion of susceptible infants who are female and become pregnant

ϕ_2: Proportion of infected infants who are female and become pregnant

ϕ_3: Proportion of treated infants who are female and become pregnant

κ_1: Proportion of $b1$ neonates who remain susceptible till $b2$

κ_2: Proportion of $b1$ neonates who remain infected till $b2$

κ_3: Proportion of $b1$ neonates who remain under treatment till $b2$

θ_1: Efficacy of the first dose of vaccine at birth

θ_2: Efficacy of the current vaccine regimen

β: Rate of infection

α_1: Rate of waning of the first vaccine

α_2: Rate of waning of the current vaccine regimen

λ: Rate of acquiring antibodies

γ_{b1}: Treatment rate of infected $b1$ neonates

γ_{b2}: rate of treatment of the infected $b2$ neonates

γ_m: Treatment rate of infected pregnant women

η_{b1}: vaccination rate of infants at the point of birth

η^*_{b1}: rate of second vaccination, after the dose at birth

η_{b2}: vaccination rate of infants classified under $b2$ on the current regimen

η_m: rate of vaccinating the pregnant nothers

References

[Pan et al., 2012] Pan, C. Q., Duan, Z.-P., Bhamidimarri, K. R., Zou, H.-B., Liang, X.-F., Li, J., and Tong, M. J. (2012). An algorithm for risk assessment and intervention of mother to child transmission of hepatitis b virus. *Clinical Gastroenterology and Hepatology*, 10(5):452–459.