Modelling Hepatitis B Vertical Transmission in sub-Saharan Africa - A Focus on the Impact of Birth Vaccination on Possible Eradication.

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0.1 Aim

To mathematically ascertain whether hepatitis B eradication is possible in the near future by focusing on preventing vertical transmission of the infection.

0.2 Research Questions

To achieve the stated aim, this research will try to answer the following question: Can Hepatitis B be eradicated from Sub-Saharan Africa (SSA) within a couple of generations, given the intervention is limited to preventing vertical transmission by administering an extra dose of vaccine at birth to the neonates, as well as treating infected mothers and their babies?

0.3 Objectives

In this research, we seek to:

1. Propose a novel deterministic SIR type model for vertical transmission which captures interventions applied to both the mothers and their newborns.
2. Check whether the interventions introduced in the model affects the population dynamics of the infected infants.
3. Ascertain the contribution of the infected infants to the disease dynamics in the general population.
4. Study the possibility of eradication by following up the results in the previous objectives stated.

0.4 Approach/Methods

The model will have two "stages":

- Stage 1: The intervention(s) applied to mothers and their babies in primary health-care settings.
- Stage 2: The model from Stage 1 will have the output called "children born with HBV infection".

This output will flow into a larger SSA birth/death model for simulation over generations. The total contribution of HBV+ children into the larger population will thus be the foundation on which the hypothesis of eradication will be shown in this work.

1 Preventing Hepatitis B Mother-to-Child Transmission

Many countries are prioritizing the hepatitis B eradication. Several articles for instance: [Andersson et al., 2015, Xu et al., 2013, Tran, 2009, Shimakawa et al., 2016] have posited that we will have to concentrate on preventing the mother-to-child transmission route if this is to be achieved in the near future. 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, it will provide an approximate 95% chance of preventing the perinatal transmission of HBV from their HBsAg-positive pregnant mother. Concerning the use of tenofovir as immunoprophylaxis for reducing HBV MTCT, a very recent study in the paper [Pan et al., 2016] has corroborated that it might be a better and possibly, safer option in the near future, as predicted by the authors in [Xu et al., 2013]. More importantly, it has been been suggested that the second dose must be administered in a very timely fashion, as a study by [Tharmaphornpilas et al., 2009] has proven that a delay in the subsequent vaccines could prove to be a hindrance in protecting the infants against the transmission of HBV.

2 HBV Mother-to-Child Transmission Risk Factors

According to [Pan et al., 2012], 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. For simplicity, the model in this document will consider the following risk factors stemming from those listed in the paper [Pan et al., 2012]: HBV DNA of pregnant women greater than $200,000$IU/mL, and pregnant women who are both HBeAg and HBsAg positive.

3 Assumptions of the Model

1. Infants below one year do not die of hepatitis b related causes.
2. no horizontal transmission in infants.
3. The intervention provides 95% efficacy.
4. Only infected mothers and those on treatment may produce infected babies.

4 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).

4.1 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

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.

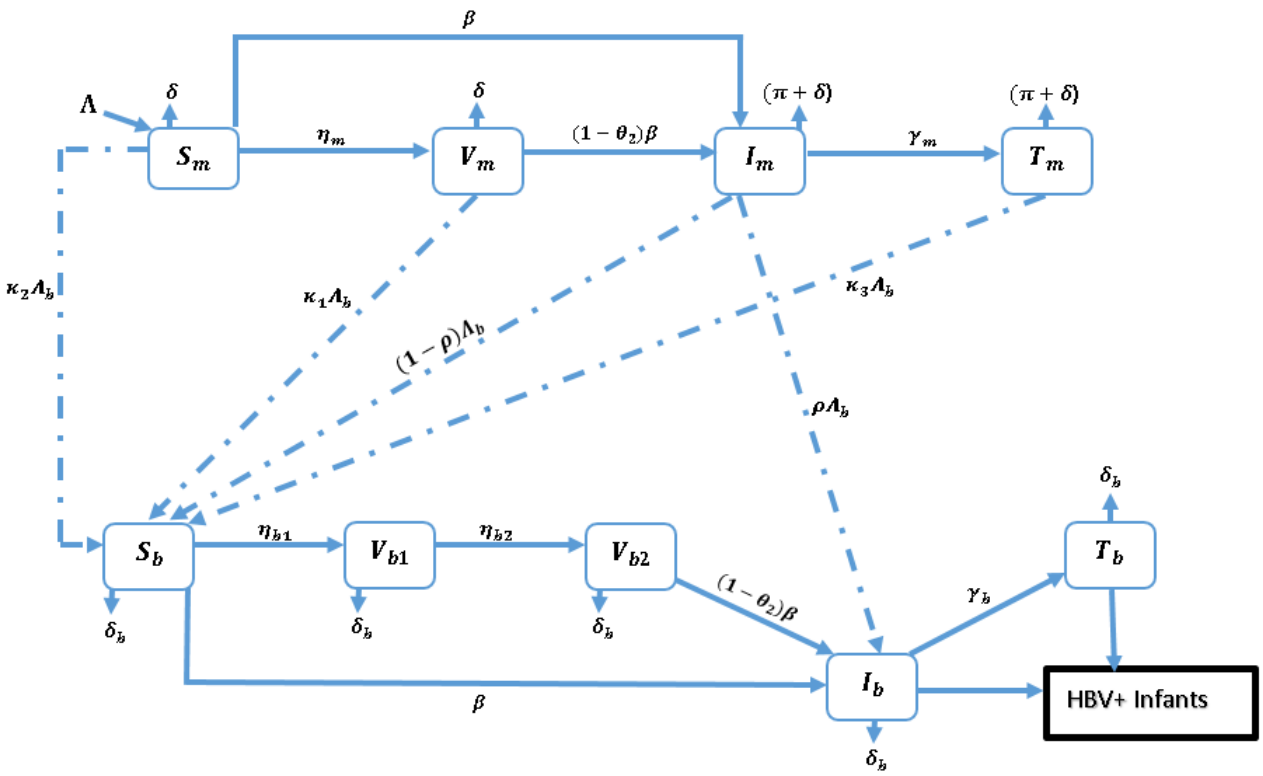

Figure 1: Shows the model structure indicating vertical and horizontal transmission. The solid arrows indicate movement of the individuals, and the dashed arrows represent births.

4.2 Description of State Variables and 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

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