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Game-Theoretical Model of Retroactive Hepatitis B Vaccination in China

Vooha Putalapattu

GAME-THEORETICAL MODEL OF RETROACTIVE HEPATITIS B VACCINATION IN CHINA

Ali Chouhan[1], Sohail Maiwand[2], Matthew Ngo[1], Vooha Putalapattu[3]

[1]Department of Biology, [2]Department of Mathematics and Applied Mathematics, [3]Department of Psychology
Virginia Commonwealth University, Richmond, VA 23284, USA

Introduction

- Hepatitis B (HepB) is one of the most common infectious diseases affecting over two billion people worldwide. One third of all HepB cases are in China.
- China made significant efforts to implement a nationwide HepB vaccination program and reduced the number of unvaccinated infants from 30% to 10%. However, many individuals still remain unprotected, particularly those born before 2003.
- A catch-up retroactive vaccination is an important and especially cost-effective way to reduce HepB prevalence .
- We analyze a game theoretical model of HepB dynamics that incorporates government-provided vaccination at birth coupled with voluntary retroactive vaccinations.

HepB overview

- HepB is transmitted through contact with infected bodily fluids such as blood, semen and saliva.
- The transmission can occur during childbirth, blood transfusion, dialysis, sharing of needle sticks, or sexual contact. In China, transmission of HepB from carrier mothers to their babies is most common.
- HepB incubation period is 60-120 days.
- An acute HepB infection lasts less than 6 months.
- There is no specific treatment for acute HepB.
- It can develop into chronic liver infection causing cirrhosis or liver cancer.
- About 10-40% of chronic HepB cases require treatment by oral antiviral agents. Almost 28 million patients in China require treatment, however, less than 2% receive it.

Scheme of HepB transmission

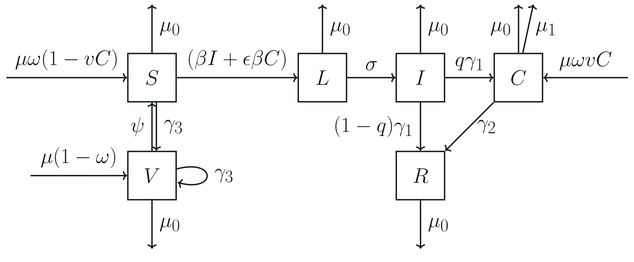

Fig. 1: Susceptible (S), Latent infections (L), Acute infections (I), Chronic carriers (C), Recovered (R), Vaccinated (V). The rates are explained in Table 1.

ODE model of HepB transmission

$$\begin{aligned}
\frac{dS}{dt} &= \mu\omega(1-vC)+\psi V - S(\mu_0+\gamma_3+\beta I+\epsilon\beta C)\\
\frac{dV}{dt} &= \mu(1-\omega)+\gamma_3 S - V(\mu_0+\psi)\\
\frac{dL}{dt} &= (\beta I+\epsilon\beta C)S - L(\mu_0+\sigma)\\
\frac{dI}{dt} &= \sigma L - I(\mu_0+\gamma_1)\\
\frac{dR}{dt} &= (1-q)\gamma_1 I+\gamma_2 C - R\mu_0\\
\frac{dC}{dt} &= q\gamma_1 I+\mu\omega r C - C(\mu_0+\mu_1+\gamma_2)
\end{aligned}$$

Symbol	Meaning	Base value
μ	Birth rate	0.0119 per year
μ_0	Natural mortality rate	$1/76$ per year
μ_1	HepB related mortality rate	7.6×10^{-5} per year
β	Effective transmission rate	10 per year
ϵ	Reduction factor for transmission from carriers	0.16
σ	Incubation rate	3 per year
γ_1	Recovery rate from acute infection	4 per year
γ_2	Recovery rate from chronic infection	0.025 per year
γ_3	Retroactive vaccination rate	≥ 0 per year
ω	Proportion of unvaccinated infants	0.1 per year
q	Probability of chronic infection	0.04
ψ	Vaccine waning rate	0.1 per year
v	Probability of perinatal infection	0.11
C_I	Cost of acute infection	\$300
C_C	Cost of chronic infection	\$40000
$C_{vaccine}$	Cost of HepB vaccination	\$3

Table 1: Parameters of HepB dynamics.

Results - Equilibria

The disease free equilibrium $E_0=(S_0,0,0,0,0,V_0)$ where

$$\begin{aligned}
S_0 &= \frac{\mu}{\mu_0}\cdot\frac{\mu_0\omega+\psi}{\mu_0+\gamma_3+\psi}\\
V_0 &= \frac{\mu}{\mu_0}\cdot\frac{\mu_0+\gamma_3-\mu_0\omega}{\mu_0+\gamma_3+\psi}
\end{aligned}$$

is stable when

$$\mathcal{R}_0=\beta\frac{\mu}{\mu_0}\cdot\frac{\mu_0\omega+\psi}{\mu_0+\gamma_3+\psi}\cdot\frac{1}{\mu_0+\gamma_1}\cdot\frac{\sigma}{\mu_0+\sigma}\left[1+\frac{q\gamma_1\epsilon}{\mu_0+\mu_1+\gamma_2-\mu\omega v}\right]<1$$

and the endemic equilibrium $E^*=(S^*,L^*,I^*,C^*,R^*,V^*)$ where

$$\begin{aligned}
S^* &= \frac{\mu_0+\sigma}{\sigma}\frac{\mu_0+\gamma_0}{\beta\left(1+\epsilon\frac{q\gamma_1}{\mu_0+\mu_1+\gamma_2-\mu\omega v}\right)}\\
V^* &= \frac{\mu(1-\omega)+\gamma_3 S^*}{\mu_0+\psi}\\
I^* &= \frac{\mu\omega+\psi V^*-S^*(\mu_0+\gamma_3)}{\mu\omega v\frac{q\gamma_1}{\mu_0+\mu_1+\gamma_2-\mu\omega v}+\beta S^*+\epsilon\beta\frac{q\gamma_1}{\mu_0+\mu_1+\gamma_2-\mu\omega v}S^*}\\
L^* &= \frac{\mu_0+\gamma_1}{\sigma}I^*\\
C^* &= \frac{q\gamma_1 I^*}{\mu_0+\mu_1+\gamma_2-\mu\omega v}\\
R^* &= \frac{(1-q)\gamma_1 I^*+\gamma_2 C^*}{\mu_0}.
\end{aligned}$$

is stable when $\mathcal{R}_0>1$.

Results - Herd immunity and Nash equilibrium

The population reaches herd immunity when the retroactive vaccination rate is

$$\gamma_{3,HI}=\beta\frac{\mu}{\mu_0}\cdot(\mu_0\omega+\psi)\cdot\frac{1}{\mu_0+\gamma_1}\cdot\frac{\sigma}{\mu_0+\sigma}\left[1+\frac{q\gamma_1\epsilon}{\mu_0+\mu_1+\gamma_2-\mu\omega v}\right]-(\mu_0+\psi).$$

The Nash equilibrium vaccination rate, $\gamma_{3,NE}$ is given as a solution to

$$\gamma_{3,NE}=\sqrt{\mu_0\psi C_{notV}(\gamma_{3,NE})}-\psi,$$

where

$$\begin{aligned}
C_{notV}(\gamma_3) &= P(S\to L)P(L\to I)\big(C_I+P(I\to C)C_C\big)\\
&= \frac{\beta I_e+\epsilon\beta C_e}{\beta I_e+\epsilon\beta C_e\mu_0}\frac{\sigma}{\sigma+\mu_0}\left(C_I+\frac{q\gamma_1}{\mu_0+\gamma_1}C_C\right).
\end{aligned}$$

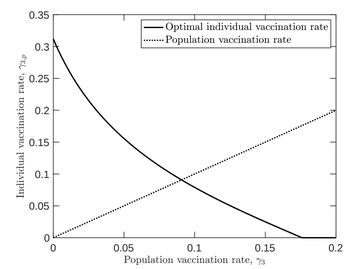

Fig. 2: The optimal vaccination rate $\gamma_{3,p}$ as it depends on the vaccination rate in the population. The point of intersection is the point of Nash equilibrium. The herd immunity is achieved when the optimal vaccination rate reaches 0.

Conclusions

- A free, nationwide catch-up vaccination program for children and adolescents in China is likely to be cost-saving and feasible.
- The herd immunity and the Nash equilibrium retroactive vaccination rates do not depend too much on the percentage of unvaccinated infants. This independence is caused by the relatively large vaccine waning rate.
- The retroactive (and repeated) vaccination is a necessary component of the HepB reduction and eradication efforts.
- There is a large difference between herd immunity and Nash equilibrium rates. The Nash equilibrium rates are in line with the vaccine waning rate; but the herd immunity rates are about 2.5 times larger.
- It is of interest to identify and evaluate other preventative measures such as behavioral modification that would have a measurable effect on the transmission of HepB.

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