Modelling the incidence and transmission dynamics of the Hepatitis A virus

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Background

Hepatitis A is an acute infectious disease caused by the hepatitis A virus (HAV). It is transmitted by the fecal-oral route either by direct contact with infected individuals, contaminated fomites, or through consumption of contaminated food or water [1]. After ingestion, uptake in the gastrointestinal tract, and subsequent replication in the liver, HAV is excreted in bile, and high concentrations are found in stool specimens [2]. The median incubation period (i.e. time from exposure to onset of symptoms) is 28 days (range 15-20 days). Peak infectivity occurs during the 2-week period that precedes the onset of jaundice and declines during the week after onset [2]. About 50% of reported patients with HAV do not have an identified source of infection [2]. Although, asymptomatic and non-jaundiced HAV-infected persons, especially children, are assumed to be important sources [2]. There is only one HAV serotype, and immunity after infection is lifelong [2]. In the US, an incremental approach to vaccination was initiated after the vaccine became available in 1995 [1].

a) b)

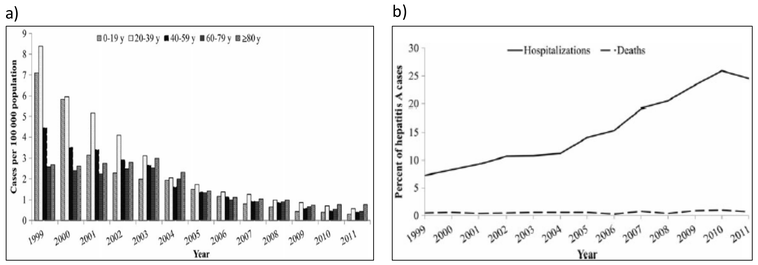


Figure 1a-b. Panel a) shows hepatitis A, incidence in the US by age group and year from 1999-2011. Panel b) displays hepatitis A-related hospitalizations and Hepatitis A-related deaths in the US by year from 1999-2011. Figures from[1]; data from the National Notifiable Diseases Surveillance System (NNDSS) and the US Census Bureau. In 2011, death certificates of decedents with HAV listed liver related conditions among frequently cited causes of death [1].

Objective

The goal of this project is to build a simple mechanistic model that can capture the incidence and transmission dynamics of the Hepatitis A virus, as captured in [1]. In particular, we are interested in making estimates of the numbers of asymptomatic Hepatitis A cases through time and identifying their role in sustaining transmission, in the US. Furthermore, given the change in the distribution of Hepatitis A cases across different age groups brought upon by the implementation of vaccination strategies, we would like to identify what further effects control strategies may have on disease burden.

Model

Transmission dynamics were modelled using a SIR model with high risk and low risk classes. The deterministic model was implemented as a system of ordinary differential equations which were numerically integrated using the 'lsoda' package in R (version 3.3.1).

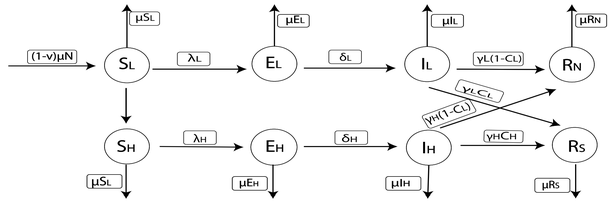


Figure 2. SIR model structure. Arrows indicate transitions between classes while the rate at which individuals move in and out of each class appears above or next to the arrows.

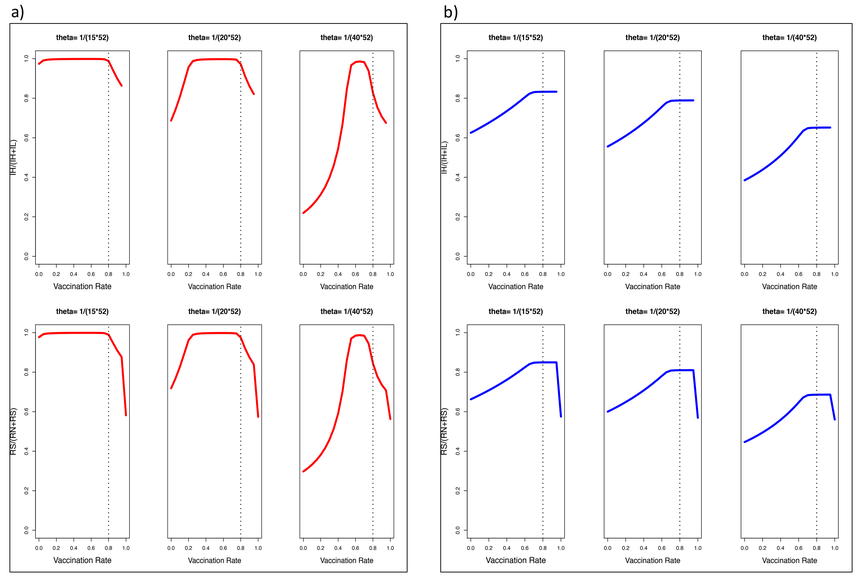
State Transition	Process	Rate
$S_L \rightarrow S_H$	movement of susceptibles from the low to the high risk class	θ
$S_L \rightarrow E_L$	exposure of susceptibles (from low risk class) to the virus	λ_L
$S_H \rightarrow E_H$	exposure of susceptibles (from high risk class) to the virus	λ_H
$E_L \rightarrow I_L$	infection of (low risk class) individuals exposed to virus	δ_L
$E_H \rightarrow I_H$	infection of (high risk class) individuals exposed to virus	δ_H
$I_L \rightarrow R_N$	recovery of infected (low risk class) asymptomatic individuals	$\gamma_L (I - C_L)$
$I_L \rightarrow R_S$	recovery of infected (low risk class) symptomatic individuals	$\gamma_L C_L$
$I_H \rightarrow R_N$	recovery of infected (high risk class) asymptomatic individuals	$\gamma_H (I - C_H)$
$I_H \rightarrow R_S$	recovery of infected (high risk class) symptomatic individuals	$\gamma_H C_H$

Table 1. State transitions for each class in the model (S, susceptible; E, exposed; I, infected; R, recovered). Individuals in each class can either be at low (L) or high risk (H) of infection. Individuals in the exposed class represent those who have been exposed to the virus but are not yet infectious. The recovered class is divided between symptomatic (RS) and asymptomatic (RN) cases. RS cases are more likely to be reported through hospitalizations or visits to primary physicians.

Parameters	Interpretation	Value(s)
β_{LL}	rate at which low risk individuals infect other low risk individuals	0-2
β_{LH}	rate at which low risk individuals infect high risk individuals	0-2
β_{HL}	rate at which high risk individuals infect other high risk individuals	0-2
β_{HH}	rate at which high risk individuals infect low risk individuals	0-2
γ_L	recovery rate for low risk individuals	0.33
γ_H	recovery rate for high risk individuals	$\gamma_H = \gamma_L$
δ_L	rate at which low risk individuals in the exposed class becomes infectious	0.5
δ_H	rate at which high risk individuals in the exposed class becomes infectious	$\delta_H = \delta_L$
μ	death rate (life expectancy equals 75 yrs.)	$1/(75\times52)$
θ	rate at which individuals in the low risk class enter the high risk class	$1/(a \times 52)$
C_H	fraction of recovered symptomatic cases	1
C_L	fraction of recovered asymptomatic cases	$0.1C_H$
v	proportion of population vaccinated	0.01-0.10
η_H	movement/migration to high risk class	5×10^{-7}
η_L	movement/migration to low risk class	$\eta_L = \eta_H$

Table 2. Parameters of the model, their meaning, and the values, or range of values assigned. Here, *a* has values of 15, 20, or 40. Values are in weeks^{-1}.

Results



Figures 3a-b. The upper row in each panel displays the effect of vaccination on the fraction of infections among the high risk class. The lower row in each panel shows the effect of vaccination on the fraction of recovered cases that are symptomatic. In panel a) mixing is assortative, $B_{HH}= B_{LL}= 2$; $B_{HL}= B_{LH}= 0$. In panel b) mixing is homogeneous, $B_{HH}= B_{LL}= B_{HL}= B_{LH} = 1$. For both models migration/movement to the low and high risk classes equals η, where $\eta= 5 \times 10^{-7}$. Force of infection equals $B_{LL} I_L + B_{LH} I_H + \eta_L$ for the lost risk class and $B_{HH} I_H + B_{HL} I_L + \eta_H$ for the high risk class. The dotted line represents the elimination threshold, i.e. the vaccination rate at which the disease is eliminated. Based on the parameters chosen, we conclude that infections from low risk individuals contribute negligibly to the number of symptomatic cases.

Future Work

Most of the parameter values used here (e.g. infectious period) were estimated from the literature. Future work should include fitting the model to the data and estimating unknown parameters. It should also incorporate seroprevalence data before and after HAV vaccination was introduced. If possible, different age-structures should be added to the model in an effort to understand the effect on age on HAV transmission.

References:
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