A simulation model of the spread of blood borne viruses through one-one contact

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Abstract The spread of a blood borne virus is not a purely random event. Its transmission is facilitated by a complex combination of behavioural and clinical factors. It is almost impossible to capture all these dimensions in an analytical model without much simplification. In an environment where it is not possible to carry out experiments, it restricts researchers to observational studies spanning decades and makes policy evaluation a retrospective exercise. This paper presents a generic stochastic micro-population simulation model with clinical and behavioural aspects. It can be used to model of the spread of blood borne viruses such as Human Immuno-deficiency Virus (HIV) and hepatitis C virus (HCV). The simulation model can be used to assess the sensitivity of the epidemic to input parameters as well as test the long-term effect of public health interventions.

1. Introduction

Since the Human Immuno-deficiency Virus (HIV) epidemic, there has been an increasing interest in the spread of blood borne viruses. As blood borne viruses are transmitted through one-one contact between individuals, modelling the spread of such diseases involves consideration of the clinical aspects of the infectious agent as well as behavioural aspects of the individuals that facilitate the transmission. This paper presents a Markovian simulation model that uses Monte Carlo simulation of the parameters and a discrete time simulation of the system over a period of decades. The objective of the study is to assess the sensitivity of the epidemic to changes in the values of the input parameters as well as quantify the impact of any interventions made through public health initiatives. The simulation model used is a stochastic micro population model with each individual handled as a separate entity with unique behavioural and clinical attributes. The model can be used to experiment with the spread of viruses such as HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV). It is developed in generic form and later applied to the spread of hepatitis C among injecting drug users.

2. The model

The system consists of a cohort of individuals who are divided into mutually exclusive geographic groups with the assumption that individuals *usually* stay within their group and interact only with others in that group. The interaction facilitates the transmission of the infectious agent and those individuals who are infected progress through the natural history of the disease over the simulated time frame.

The main characteristics of the model are as follows:

i. The population is open; there new arrivals to and departures from the cohort as well as movement between groups throughout the simulation,

ii. The system is Markovian with every individual being in one, and exactly one, of the set of clinical states of the disease at any given time period,

iii. Each individual has a unique transition matrix that gives the probabilities of transition from one state to another in a single time period,

iv. Within each geographic group, there are a number of contact groups. These groups are used to identify contact networks for the purpose of defining interactions between individuals. Individuals may interact in more than one contact group. They may also choose to interact with only some individuals in a contact group.

v. Each individual has a set of unique behavioural characteristics that define his/her behaviour through the simulation,

vi. Contact between two individuals, leading to possible transmission of the agent, is uniquely simulated,

vii. The level of risk individuals are exposed to, based on the nature of the contact made is quantified in relative terms.

viii. The relative degree of infectiousness of infectives during various stages of the illness is included thus allowing for non-infectious periods for the infected,

ix. Individuals have parameters relating to susceptibility, immunity and treatment that can be used to test immunisation strategies, treatment programmes etc.

5.2.7. Calculating probabilities:

a) Calculating the probability of a susceptible choosing to inject in a particular contact group during a day (time unit = 1 day):

Let X be a susceptible in demographic group G1.
let X_f = contact frequency of X
(number of interactions per week).
X_s = contact spread of X
(number of contact groups associated with)
$X_c = \{C_1, C_2, C_3 \ldots\ldots C_s\}$ = set of contact groups used by X (contact pattern)

If X does not inject daily, then the first injecting day is chosen randomly from the interval [1, INT(7/ X_f)]. If X does inject daily, the first day of injecting is time t=1. Subsequent injecting days are assigned using the time between contacts calculated from X_f.

If X chooses to inject during time t to t+1, then the probability of X choosing to inject in contact group C_n = 0 if $C_n \notin X_c$
= $1/X_s$ if $C_n \in X_c$

Example:

If $X_f = 3$; (on average injects 3 times a week)
$X_s = 2$; (interacts with two contact groups)
$X_c = \{C_1, C_4\}$

Time between interactions = 7/3 = 2.3 days.
=> prob(1st day) = 1 / 2.3 = 0.43
prob(2nd day) = 1 / 2.3 = 0.43
prob(3rd day) = 1 - 0.86 = .14

First injecting time period is randomly chosen from [1,2,3];
If the first day of injecting is t=1,
the next is t = 1 + 2.3 = 3.3 = day 3
the next is t = 3.3 + 2.3 = 5.6 = day 6
the next is t = 5.6 + 2.3 = 7.9 = day 8

If X chooses to inject, then the probability of each contact group being chosen:
$P(C = C_1) = 0.5$
$P(C = C_4) = 0.5$

b) Calculating the probability of infection through a specific contact:

Let X be a susceptible and Y an infective who belongs to the same contact group, C, as X during time t to t+1.

let X_v = contact volume of X.
N_C = number of individuals in contact group C during time t.
p = probability of infection from a contaminated needle stick injury or other malpractice during a single contact with an infective;
X_ψ = susceptibility (index) of X;
X_ω = immunity (index) of X;
Y_η = infectivity (index) of Y at time t;
χ_c = environmental hazard factor of contact group C;

During a single interaction, the probability of X choosing to interact with the infective Y = $1 / (N_C - 1)$

Hence the probability of X becoming infected from a single contact with Y between time t and t+1 = $p.X_\psi.(1-X_\omega).Y_\eta.\chi_c$

Example: If $p = 0.03$;
$X_\psi = 1$;
$X_\omega = 0$;
$Y_\eta = 1$;
$\chi_c = 0.5$;

The probability of X becoming infected by Y between t and t+1
= $p.X_\psi.(1-X_\omega).Y_\eta.\chi_c$
= 0.03 x 1 x (1-0) x 1 x 0.5 = 0.015.

In the event that X was immunised with a vaccine that was 85% effective, $X_\omega = 0.85$.

Hence, the probability of X becoming infected by Y
= 0.03 x 1 x (1-0.85) x 1 x 0.5 = 0.002.

c) Calculating the probability of moving to other states of the disease:

Let X be an infective in state i. The probability of X moving from state i to state j between times t and t+1 = $T_{ij}.(1-X_\tau)$, $j > i$
where T_{ij} = transition probability from state i to state j
X_τ = treatment effect of X

Example:
Let X be in state 3, sero(+)PCR(-), and taking a treatment which slows the progression of the disease by 40%. If the transition probability from state 3 to 4 is 0.05, then the probability of x moving from state 3 to state 4 during time t and t+1 = 0.05 x (1-0.4) = 0.03

3. The simulation program:

The simulation model used in this study is a stochastic micro population model with each individual handled as a separate entity with unique behavioural and clinical attributes. The demographic and contact group structure arises from some of these individual attributes as well as giving the modeller the option of dividing the population into geographical groups.

The computer program generates a cohort of injecting drug users based on default or user given parameter settings and simulates the spread of HCV within this group over a predetermined time period. At the end of the simulation it measures the effect of various input parameters on the epidemic.

The simulation is a visually interactive program that allows the user to advance the simulation clock in single time periods, giving the ability to make interventions at any time period, or alternatively run the simulation right through to the chosen time. The period of the simulation cycle corresponds to a day. Once the simulation program has terminated, the spreadsheet interface reads the output

files generated. These output files are then used to plot graphs of output parameters and also calculate performance measures for the model.

The events simulated on a daily basis for each individual in the cohort include individuals choosing to inject, choosing a contact group to inject in, interacting/making contact, infection, transition to other states of the disease for those already infected with the virus, migration into and out of the system, inter-group movement and interventions such as behavioural changes and treatment.

The model uses a system of holding bays to house individuals during non-injecting and injecting periods. Each group has a base holding bay where individuals are kept until they choose to interact (inject) in a particular contact group. A holding bay for each contact group is used to separate individuals for interactions. Each susceptible is allowed to make contact with their "contact volume", the average number of individuals they choose to interact with, with each contact chosen randomly from the contact group. The proportion of susceptibles and infectives chosen for contact is implicitly determined by the current prevalence level of the disease within the contact group. After interaction, a susceptible is returned to the holding bay. The infected individuals are then considered in order to simulate possible transitions to other states of the disease. Apart from the above, migration to and from each group including inter-group movement is simulated using group parameters. Unless an individual has a specific intervention order to migrate, individuals who migrate are picked randomly. Any interventions that are listed for the corresponding time period are then implemented before the cycles begin again.

The cohorts used in the simulation were generated using empirical distributions of parameters observed in the Victorian Injecting Drug Users Cohort. In cases where actual values were not available, suitable ranges were chosen for parameter values. These values were then varied to assess the effect on the output measures.

The program generates the simulated probability distributions of the following output measures:

1. the end prevalence of each group,
2. the mean time taken for a susceptible to become infected,
3. the mean number of infections hosted by an infective,
4. the epidemic chain (generations) and
5. mean number of safe contacts (contacts that did not lead to infection) before infection.

3. Results from application to hepatitis C:

The model was applied to the spread of hepatitis C among injecting drug users. A sample of the results obtained is presented below.

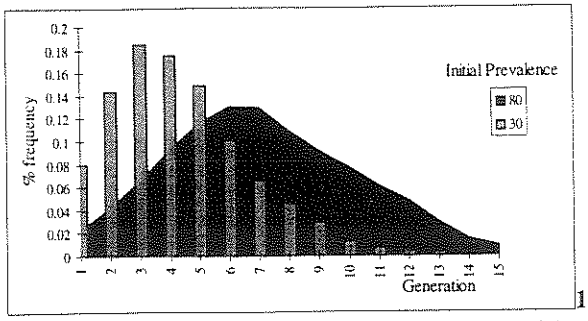

Figure 1: Comparison of the simulated distribution of the generation of infectives with the initial prevalence set at 30% and 80% and the Probability of infection = 0.03.

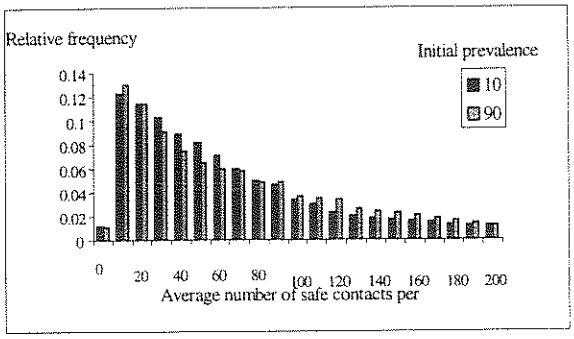

Figure 2: Simulated distribution of the average number of safe contacts made by susceptibles.
Probability of infection = 0.03.

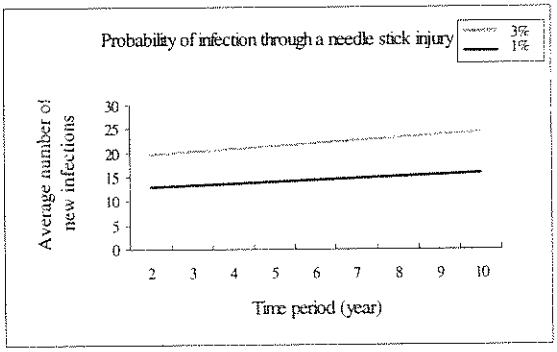

Figure 3: Comparison of the effect of the bore size of needles used (Fitted data)
Initial prevalence = 70%.

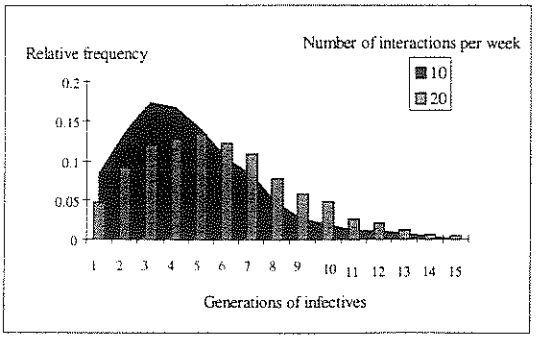

Figure 4: The simulated distributions of the generations of infectives.
Initial prevalence = 70%; probability of infection = 0.03.

4. Conclusions

The model presented here is very limited by the scarcity of accurate data. The lack of information on some of the behavioural aspects as well as inability to even approximate some of the parameters clearly limits the use of the model. But, even during the period of this study, there has been a constant flow of new research providing new insights into HCV. It has been necessary, for the purpose of completing the thesis, not to keep including the continuous new supply of data but to cut off at some point. As it stands the usefulness of the model is not so much as a forecasting tool but more as an experimentation tool, to be able to change parameters values and assess the impact on the epidemic. It will enable strategies to be implemented which meet the best achievable objectives.

As the primary objective of this study was to model transmission of the virus, the initial state of the cohort was set so that all individuals who are infected are also infective. This is obviously unrealistic as, whilst the prevalence of HCV among IDU's is about 70%, it is clearly not the case that 70% of the IDU population are infectious. Some of the infected individuals are likely to belong to the subset who are classified as removals, whilst some are likely to be in hospitals and hence not be in contact with the rest of the IDU community. While it is necessary to introduce a more representative infected population this data is presently unavailable.

A useful extension to the model would be an economic perspective, in order to asses the economic cost of the epidemic and the effectiveness of public health policy. As the simulation model is able to assess the effect of interventions to the parameters in terms of the progression of the disease, it can be easily linked to a health economics submodel. By attaching a financial value to various interventions such as drug education programs and changes to needles issued, it is possible to evaluate the resulting financial effect through the estimated savings to Medicare in the long term with less individuals needing expensive medical attention such as transplants.

The spread of a blood borne infectious agent such as HIV or HCV is facilitated by a complex combination of behavioural and clinical factors. It is almost impossible to capture all these dimensions in an analytical model without much simplification. In a environment where it is not possible to carry out experiments, it restricts researchers to observational studies spanning decades and makes policy evaluation a retrospective exercise. But, with the computer technology available today, it is possible to build a very realistic computer simulation model that includes key features of such a dynamic setting. The computer simulation model developed in this study demonstrates the usefulness of simulation modelling in epidemiology.

5 Acknowledgements

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