International Journal of Current Research and Modern Education (IJCRME)
Impact Factor: 6.925, ISSN (Online): 2455 - 5428
(www.rdmodernresearch.com) Volume 5, Issue 1, 2020

MODELING INFECTIOUS DISEASE: DETERMINISTIC AND STOCHASTIC SACR MODELS

Wudneh Ketema Moges
Lecturer, Department of Statistics, College of Natural and Computational Science, Debre Berhan University, Debre Berhan, Ethiopia

Cite This Article: Wudneh Ketema Moges, "Modeling Infectious Disease: Deterministic and Stochastic SACR Models", International Journal of Current Research and Modern Education, Volume 5, Issue 1, Page Number 27-34, 2020.

Abstract:

Infectious diseases have been a great concern in human community. The transmission of hepatitis C occurs primarily through injecting drug user and it is mainly associated with the sharing of contaminated syringes or needles, although evidence for risk of hepatitis C infection through sharing of other injecting equipment is increasing. To measured seroprevalence of hepatitis virus (HCV) infection among injection drug users (IDU) using deterministic and stochastic models and investigate how the model parameters depend on the population size. The mathematical model quantiles the transmission of Hepatitis C among IDUs in the population. From the compartmental models, the frequency of sharing injecting materials has an impact on the force of infection and the prevalence of HCV.In this report the SACR model are great rule in mathematical model. So, from these case to describe the transmission dynamics of hepatitis C in populations of IDUs can help to identify those parameters and pieces of information that are needed to understand the of hepatitis C.

Key Words: Hepatitis Injecting Drug user (IDU), Compartmental Model, Stochastic & SACR model.

1. Introduction

Infectious diseases have ever been a great concern of human kind. Hepatitis C is an infectious disease affecting the liver, caused by the hepatitis C virus (HCV). The infection is often asymptomatic, but once established, chronic infection can progress to scarring of the liver (fibrosis) and advanced scarring. Millions of people die annually from measles, malaria, tuberculosis, AIDS and billions of others are infected. The Hepatitis C Virus (HCV) is an infectious disease which spreads through blood contact. The features of HCV infection that make it hard to combat are that a large fraction of all infected individuals become chronic carriers of the virus and about 170 million people are chronically infected with HCV worldwide [1].

HCV is transmitted primarily through percutaneous exposure that can result from injection-drug use, needle-stick injuries, and inadequate infection control in health-care settings. Much less often, HCV transmission occurs among HIV-positive as a result of sexual contact with an HCV-infected partner [3], non-professionally applied tattoos and among infants born to HCV-infected mothers. With an estimated 3.2 million chronically infected persons nationwide, HCV infection is the most common blood-borne infection in the United States.

There are two models applied in infectious diseases modelling.They are Mathematical Models and Stochastic Models .In the stochastic model approach, the epidemic is considered as a chain of events (Acute infections, Chronic carrier, recovery) occurring at random times among individuals. According to this approach taken into account the randomness of durations of the different health stages in the population. At each event, the transition that occurs is determined by probabilities induced by the global transition rates.

Mathematical modeling is an alternative approach; indeed, it enables to give an estimation of the efficiency and cost of multiple strategies of harm reduction, screening and treatment effects upon HCV transmission within a short period of time. The main goal is to review mathematical models used to simulate transmission of HCV among PWID, and to evaluate their pros and cons.Mathematical models used in the articles were divided into two categories: compartmental models and individual-based (or agent-based) models (IBMs).

Compartmental models were the most frequently used class of models for HCV epidemic simulation. They considered transmission of HCV infection at the macroscopic scale, dividing the population into compartments corresponding to different states of the infection process: susceptible, acute infectious, chronic carrier, recovered. [4, 5]. Transitions from one state to another were based on rates that could be time dependent. The change in the estimated number of HCV infections through time has been used to calculate the growth rate and the basic reproductive number, R0, of HCV (Pybus et al., 2001). R0 is the number of secondary infections generated by a single infectious individual at the beginning of an epidemic. Where an epidemic is initiated by the introduction of an infection into a large susceptible population, R_0 reflects the intrinsic replicative capacity of the infection (Anderson and May, 1991).However, the models used to estimate R_0 from genetic data assume that the host population size remains constant through time (Pybus et al.2001).

2. Objective:

The objective of this research is to measured seroprevalence of hepatitis virus (HCV) infection among

injection drug users (IDU) using deterministic and stochastic models and investigates how the model parameters depend on the population size.

3. Data:

In this research, the data sets reporting seroprevalence of HCV among IDUs are considered the total population of N = 1 individuals. The force of infection and the rate, at which susceptible individuals became infected, was estimated in the first instance including exposure time as the only covariate. The exposure time, i.e. the period of time the IDU is considered to belong to the risk group, is defined as the time interval (in years) between the age at first injection and the age at test. In the second instance, the force of infection was calculated including, in addition to Exposure time, needle sharing, sharing other injecting materials, age at first injection, gender and location. The variable location was included because it was previously demonstrated that Hepatitis C prevalence among IDUs is mainly subject to geographic variation. The initial number of Acute infective (AI_0 = 0.003) is introduced within a fully susceptible population of (S_0 = 0.997) individuals giving rise to the total population of (N = 1) individuals. The duration Dependent force of infection, (t), with the basic reproduction number.

Description of the Data:

Table 1, depicted that the positive and negative value of HCV in relation to variables. There is high positive HCV value in share needles to other, so share needles to other is a high risk factor. The variable gender of male is high positive HCV value to compare gender of female. The prevalence of HCV in IDUs sharing other materials is, conditional on sharing syringes and location, higher for every period of injecting drug use than among IDUs not sharing other materials. The variable share others is a high positive HCV value compare to the negative HCV value of share others. The proportion of drug users infected with HCV increases with longer duration of injecting drug use. The force of infection clearly depends on the duration of injecting drug use. The duration of IDU is high positive value HCV value in the year one to two years.

Table 1: Distribution of Variables for Hepatitis C virus injecting drug users

Variables	Category	HCV Positive	HCV Negative
Share Needles	Yes	240	40
	No	85	56
Gender	Male	226	68
	Female	98	28
Share Others	Yes	274	66
	No	51	30
Infection IDU	Yes	325	0
	No	0	96
Location	one	325	96
Index	0	129	62
	1	196	34
Ever Injected	Yes	325	96
	No	0	0
Duration IDU	1 or less Year	0	7
	1 to 2 Year	88	49
	2 to 3 Year	9	0
	3 to 5 Year	60	17
	6 to 10 Year	63	11
	> 10Y ear	67	7
	Total	325	96

4. Methodology:

In this section, two types of models were used for the study of the infectious diseases at the population scale. The description of deterministic models and stochastic models were discussed below. In both model families, the basic SACR model were considered, with the assumption that the total size of the population **N** is constant and the population is open (i.e. births and deaths), as we were interested in the short-term dynamics of an epidemic. Models are simplified representations of reality and are used in many areas of science, finance and industry. When a model includes a probabilistic component is called a stochastic model (Lindsey; 2007). Stochastic modelling has been a very active area of research, taking into account the nature of the outcome variable and explanatory variables.

Deterministic Model:

A mathematical model describes the spread of an infectious disease in a well-defined population and also known as compartmental models, A compartmental model is used to represent the dynamics of infection for HCV to attempt that describe and explain what happens on the average at the population scale. They fit well

large populations. These models categorize individuals into different subgroups (compartments). The SACR model, for example, includes four compartmentsrepresented by the Susceptible, Acute infectious, chronic carrier and Recovered. Between those compartments we have transition rates which tell us how the size of one compartment changes with respect to the other. The best known transition rate is the force of infection or the attack rate which measures the rate at which susceptible becomes infected. In deterministic models, population size of the compartments are assumed to be functions of discrete time *t = 0; 1; 2*; .or differentiable functions of continuous time. This enables us to derive sets of difference or differential equations governing the process. The evolution of this process is deterministic in the sense that no randomness is allowed.

In this paper from different compartment model we only used SACR compartmental model a model in which they considered an open population with only four compartments: susceptible, acute infection, chronic carrier C and Recovered. The compartments used for this model consist of four classes. These are susceptible S, acute infection A, chronic carrier C and Recovered R.

- S(t): is used to represent the number of individuals not yet infected with the disease at time t, or those susceptible to the disease.
- A(t): is the number of chronic carriers .
- C(t): denotes the number of individuals who have been infected with the disease and are capable of spreading the disease to those in the susceptible category.
- R(t): is the compartment used for those individuals who have been infected and then removed from the disease, either due to immunization or due to death. Those in this category are not able to be infected again or to transmit the infection to others.

Designing Deterministic Model of Hepatitis C Disease:

The important stages of a hepatitis C infection are acute infection, chronic carrier state, and recovery (viral clearance).It seems that there is no complete lasting immunity for those who were able to clear the virus, but that individuals may contract subsequent infections. A compart mental model is used to represent the dynamics of infection for HCV as the population is subdivided into a number of subsets according to the most important stages of HCV. We denote the number of susceptible by S, the number of acutely infected individuals by A, the number of chronic carriers by C and the number recovered by R. The individuals are recruited into the susceptible class by the quantity B, and the mortality rate (naturally) given as. The susceptible hosts are infected by the acute infection class with a force of infection λ which depends on the rate of borrowing injecting equipment *k*, and the transmission rates (probabilities ba, bc).

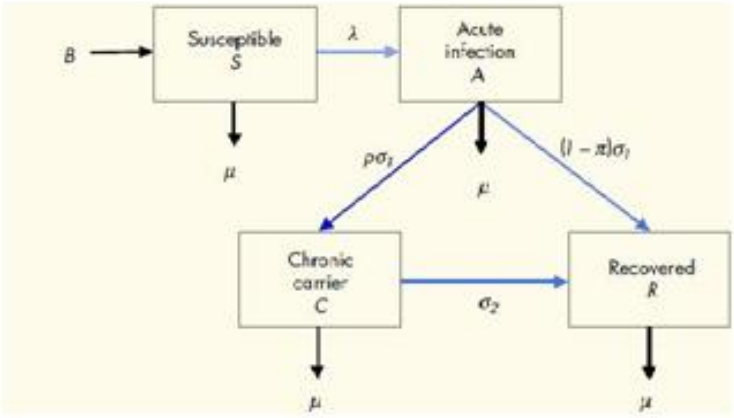

Figure 1: Flow chart of a simple hepatitis C model

From the above Figure 1we observed that, ba is the transmission probability per contact, if individual was in its primary acute infection and bc is the transmission probability per contact, if individuals was a chronic carrier. An individual with primary acute infection was move out of that state with rateδ_1 , with a fraction p becomes chronic carriers and the remaining fraction, (1-p) recovering completely. Chronic carrier individuals can still clear the virus with rate δ_2 and move into the recovered state for open population the total population was calculated as:

$$N = S(t) + I(t) + C(t) + R(t) \quad \text{(4.1)}$$

For a model formulated in terms of proportions with natural birth and death rates μ and force of infection $\lambda(t)$, the equations for SACR model are given by:

$$\frac{dS}{dt} = \beta - \lambda S(t) - \mu(t)S(T)$$

$$\frac{dI}{dt} = \lambda S(t) - \delta 1 A(T) - \mu(t)$$

$$\frac{dC}{dt} = p\delta 1 A(t) - \delta 2 C(t) - C(t)$$

$$\frac{dR}{dt}=(1-P)\delta 1A(t)+\delta 2C(t)-\mu R(t)$$

Then, the proposed duration –dependent force of infection given by:

$$\lambda(t)=k(ba\frac{A(t)}{N(t)}+\text{bc}\frac{C(t)}{N(t)})\_\_\_\_\_ (4.2)$$

The time window was chosen in months since disease specific parameters and demographic parameters values are based on monthly measurements .To calculate the duration dependent force of infection,$\lambda S(t)$with N=1 (non-dimensional zed) as the population size . The duration dependent force of infection was estimated for Hepatitis C at different contact rates for *k* values, for an open population in which the flow of individuals in to the population is N. In fact, science

$$r_{(t)=1-S(t)-a(t)-c(t)}$$

is the dynamical behavior of system.

HCV Transmission Models on IDUS:

Based on the natural course of the infection, the model considers three disease stages acute infection, chronic carrier and recovered. At this point there was a lot of uncertainty about secondary infections so the authors did not consider them in the model.SHCV denotes the number of susceptible, IHCV the number of acute infectious individuals, CCHCV the number of chronic carriers and RHCV the number of recovered. The force of infection depends on the rate of borrowing injecting equipment k and the transmission rate. If a susceptible individual borrows equipment from a someone with acute infection the transmission rate is denoted, and is denoted by CC if the infectious individual is a chronic carrier. To account for the heterogeneous behavior of the injecting drug users, the model can be extended assuming that there are two subgroups in the population. One of the subgroups with a high average rate of needle sharing and one with a low rate. The authors assume that the subgroups differ in their behavior but not in the disease specific parameters and all the people entering to specific risk group will remain there during their entire injecting career. The time at risk is actually the duration of injection reflecting the exposure time of the individuals during their injecting career.

Stochastic Models:

The chance of variation in the risks of exposure, disease, and other factors. They provide much more insight into an individual level modeling and stochastics models was used. The population or sub populations involved are too small population size where every individual plays an important role in the model. Hence, they are used when known heterogeneities are important as in small or isolated populations. Stochastics models have several advantages. More specifically, they allow close watching of each individual in the population on a chance basis. They can be laborious to set up and need many simulations to yield useful predictions. These models can become mathematically very complex and do not contribute to an explanation of the dynamics **R_0** is the basic reproductive number, which is the mean number of secondary infections that is caused by in single index throughout his/her infections period when introduced in a fully susceptible host. Is often considered as the threshold quantity that determines when an infection can invade and persist in a new host population. It will be shown that when $R_o \leq 1$, the mean of the probability distribution for the number of infective monotonically decreases to zero. It is also known that when $R_o>1$, the probability distribution for the number of infective is bimodal for a long period of time.

An individual is followed over time for the occurrence of a specific event (recovery, death, infection). The main outcome is the time to the event and typically we are interested on estimating the time until the event happens (survival function) or the event risk (hazard function) and assessing the impact of covariates.

$$\Lambda(t)=\int_0^t \lambda(t)d(t)\_\_\_\_\_ (4.3)$$

And $\pi(t)$ the probability to be infected before exposure time, then

$$\pi(t)=exp(-\Lambda(t)$$

A generalized linear model (GLM) in which the probability to be infected is given by $\pi(t)=1-\exp(-\alpha t^{\beta})$ for the Weibull AFT model to find the force of infection can be calculated by $\lambda(t)=\frac{\pi(t)}{1-\pi(t)}$ hence the force of infection for the Weibull model is given by $\lambda(t)=\alpha\beta t^{\beta-1}$ and the important covariate included in the model, so the probability to become infected prior to exposure time is $\pi(t)=1-\exp(-\alpha t^{\beta}\exp(Zy))$

Finally the Weibull force of infection is:

$$\lambda(t|z)=\alpha\exp(Zy)\,\beta t^{\beta-1}\text{-}\_\_\_\_\_ (4.4)$$

Software:

The mathematical and stochastic models of the result were used to analyze based on different mathematical and stochastic software. For the mathematical software, MATLAB and R studio for version 3.6.3 were used to run simulations and fit the mathematical models including difference, differential equations and DTMC models.

5. Results:

Under this section we have discussion to describe the data, in ordered to address the objective of this paper for both deterministic and stochastics models based on the data.

Deterministic Compartmental Model:

In the first mathematical model we used the models for Hepatitis C among injecting drug users (IDU). The duration of acute phase of infection is estimated at around two months. It is estimated that the fraction of acutely infected persons who becomes chronic carriers is around 80%, that is the disease specific parameters i.e. ***ba,*** $bc, \delta 1, \delta 2$ were defined in the model, but not changed i.e. ba =0.3, bc=0.03, $\delta 1 = 5, \delta 2 = 0.01$ and somehow reflects reality. According to (Kretzschmar and Wiessing, 2006) of the given value of the parameter to calculate the force of infection is given by:

$$\lambda(t) = 10(0.3 * \frac{0.03}{1} + 0.03 * \frac{0.03}{1})$$

$$\lambda(t) = 0.909$$

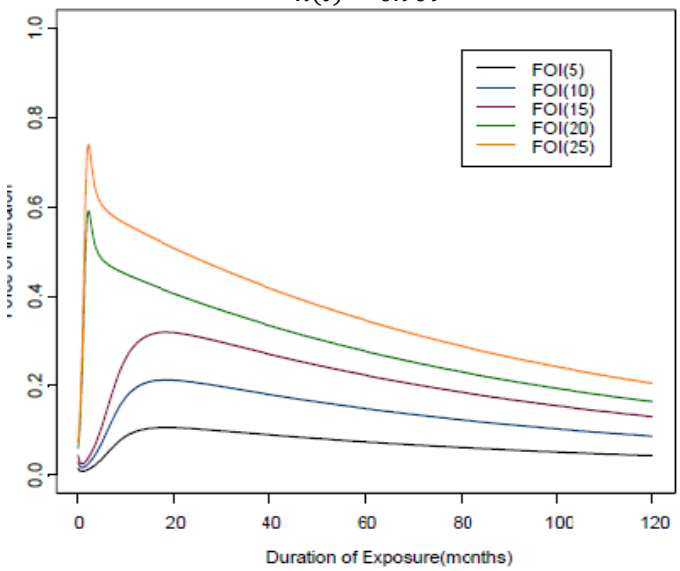

Figure 2: The force of infection at different frequency of *K* contacts

From the above Figure 2, we explore that for a different value of *k* is shows that the estimated forces of infections at different values of the frequency of sharing injecting materials, *k*. a very steep increase in the force of infection at shorter durations for higher sharing frequencies (k = 25, 20). For lower sharing frequencies i.e. k = 5, 10, 15, the force of infection rises steadily over the du-ration of exposed. In all circumstances, the force of infection declines after reaching the peak but it does not diminish to zero yet after 120 months of exposure.

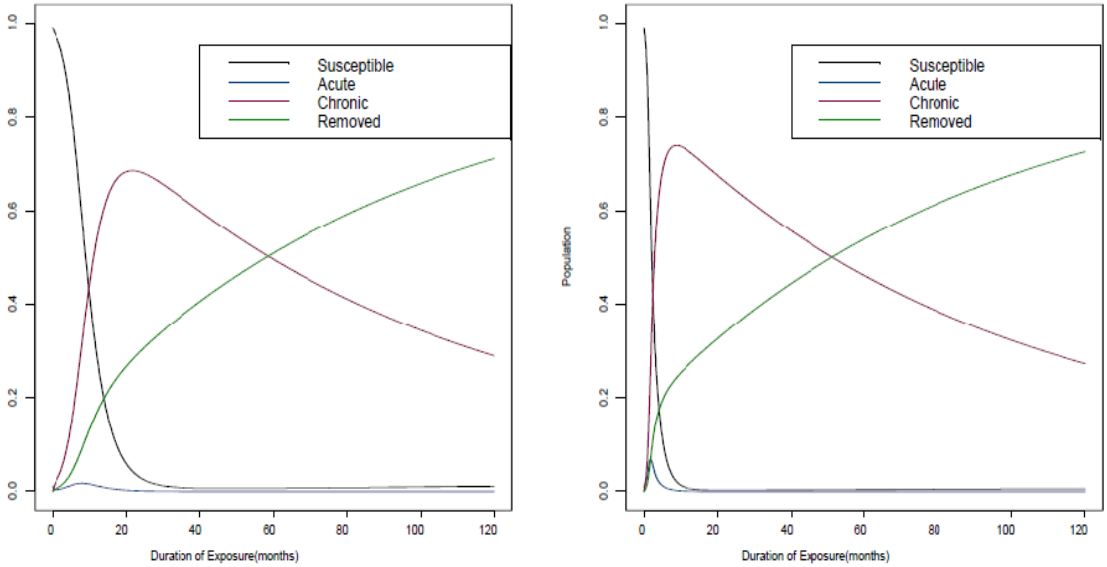

Figure 3: SACR for k=10and k=20

From the above Figure 3, we depicted that the duration – dependent force of infection was estimated by the model at different contact rates k. From the diseases parameters were held constant and *k*varied from 10 to 20. One can observe small proportions of the population who had acute infection. Proportions of infected individuals who are chronic carrier's increases to peak of almost 70% of the population size within duration of approximately 20 months and declines in some way because of the recovery rate which is almost 1% over a long duration. The proportion of individuals recovering increases steadily and becomes larger than the proportion of

the carriers after almost 60 months (5 years) over the total duration of exposure. Compared to figure on the right panel, where k is doubled to 20, at almost 12 months (1 year) the dynamics are steeper for the acute, chronic carrier and recovery states at shorter duration of exposure. The rate of infections in each state are higher when k = 20 at shorter duration of exposure than when k = 10. This might indicate that the frequency of sharing injecting materials have an force on the transmission of Hepatitis C within a population of IDUs whiles the transmission probabilities do not change over time or perhaps independent.

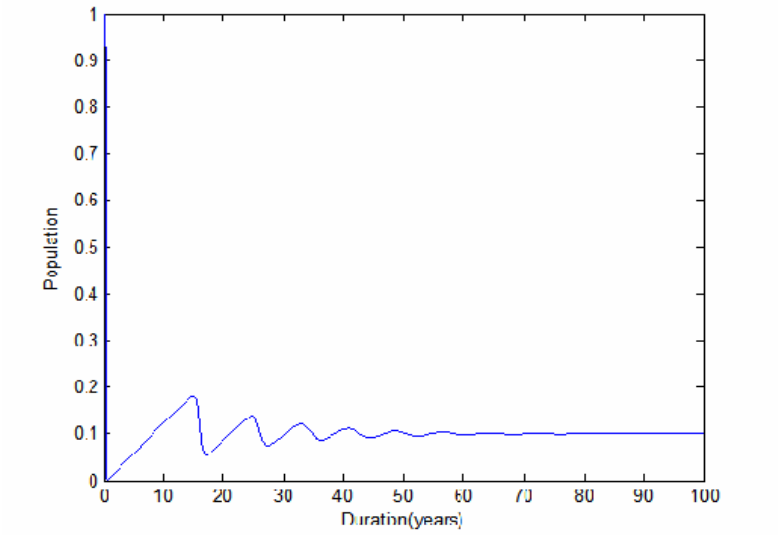

Figure 4: Susceptible with no transmission

From the above Figure 4, we examine that initial epidemic is followed by an episode in which the pool of susceptible is restocked by births, during this period a new epidemic is triggered after time approximately 15yrs when the proportions of the susceptible is almost 20%.We observe that there is an increase of chronic infection in the population. The second epidemic is less severe because the bulk of the population is immune, successive epidemics are less and less severe

A Heterogeneous Population:

There are IDUs who scarcely ever share injecting equipment and others who share very frequently. Therefore, one would like to take that heterogeneity into account in the model and explore its consequences. We expand the above model by assuming that there are two sub-groups in the population, one with a high and one with a low average rate of needle sharing. We assume that the two subpopulations differ in their behavior and in their mortalities, but not in the disease-specific parameters. A fraction, V, of all persons entering the population belongs to the low-risk group and the remaining (1-V) to the high –risk group. Individuals stay in that risk group during their entire drug using career. Mortalities can differ between low and high risk groups, i.e. we have parameters $\mu 1\ and\ \mu 2$ for the low and high-risk groups respectively. When the demographic process is at equilibrium, a constant fraction of the population is in group determined by $\beta, V, AND\ \mu i$.

6. Stochastic Models:

In this section, was considered included only the exposure time as a covariate and the smaller AIC value for the better the model fit, so the Weibull model is the better fitted model, with the deviance for this model is 419.38 on 419 degrees of freedom which indicates acceptable goodness-of- fit. The deviance for this model is 360.58 on 400 degrees of freedom indicating a good fit of the model.

Parameter estimates of the final model are shown in Table below. Note that the age at first injection was not found to be significant and was therefore omitted from the final model. The prevalence of HCV among IDUs sharing syringes or needles, conditional on location and sharing other materials, increases faster than among IDUs not sharing syringes or needles but reaches, after 25 years of injecting drug use, approximately the same level.

The parameter estimate for sharing other materials equals this indicates that, adjusting for other covariates in the model, the HCV prevalence among IDUs not sharing other materials is significantly lower compared with the HCV prevalence among IDUs sharing other materials. As the interaction between exposure time and sharing other materials was not found to be significant, the force of infection, at each exposure time, of IDUs sharing other materials is higher than the force of infection of individuals not sharing other materials. So from this case, the above explained variables of the study do not include the final Weibull models. The proportion of drug users infected with HCV increases with longer duration of injecting drug use. The prevalence of HCV increases very steeply until about 4.5 years of injecting drug use, while after 4.5 years of injecting drug use the prevalence rises more slowly. The median duration of injecting drug use at infection.

Duration of Drug Injection:

There are 7 categories for duration of injection: 1 year or less, 1 year to 2 year, 1 year to 3 year, 2 year to 3 year, 3 year to 5 year, 6 year to 10 year and greater than 10 year. Due to the small number of individual's population. Clearly the acceleration factor for injecting any drug as compared to not injecting is very high. The results of the models are shown in table below. The baseline class is no recent injections. For instance, the acceleration factor for 1 year to 3 year is $exp(-8.78) = 1.54$ that is the median time to HCV infection for the IDUs with no recent injections is two times the median time to HCV infection of those who inject drug.

Duration Dependent Force of Infection:

In this section we include calendar time of the first injection as a covariate in order to investigate if the risk of IDU to be infected changed with time. We consider a categorical variable with six times categories. Assuming a Weibull baseline hazard shows the best fit to the data according to the AIC values.

$$\begin{cases} 1year\ or\ less \\ 1year\ to\ 3\ year \\ 2year\ to\ 3\ year \\ 3year\ to\ 5\ year \\ 6year\ to\ 10\ year \\ above\ 10\ year \end{cases}$$

The parameter Estimates for the generalized Weibull model are shown in Table 2 below, the acceleration factor for the IDUs with first injection in 1 year or less compared with IDUs who first inject in 1 year or less equals zero. Hence, the median HCV infection time for the IDUs starting to inject in 1 year or less, so from this we conclude that the force of infection clearly depends on the duration of injecting drug use.

Table 2: Single Covariate Weibull Parametric Models

Parameter	n	Estimate and SE	p-value	HR	95%HR
Intercept	-	4.6(0.45)	0.001	-	-
IDU 1year or less	74	0.00(-)	-	1.00	-
IDU 1year to 3year	148	-8.78(0.76)	0.0013	2.32	(-7.34,4.15)
IDU 2year to 3year	36	-0.56(0.35)	0.0034	2.4	(-5.6,4.15)
IDU 3year to 5year	878	-0.956(0.26)	0.0005	2.6	(0.524,4.3)
IDU 6year to 10year	74	-1.2(0.004)	0.0003	3.2	(1.82,5.96)
IDU above 10year	47	-0.76(0.012)	0.002	0.47	(0.83,8.5)

7. Discussions:

In this paper , the SACR Model which used to model infectious diseases by computing the amount of people in an open population at different compartments *(Susceptible, Acute infectious, Chronic carrier and Recovered.)* at a given period of time were explored by using deterministic and stochastic approaches. The mathematical models fitted were presented [1] .We assumed that the Homogeneous population of IDU's for the show of HCV. The results showed that early drug users may have a high risk of being infected with HCV based on the Frequency of borrowing injecting materials or rates of contacts. The force of infection for the population varying rates of borrowing injecting materials,i.e. Assume the value of k =1, 5, 10, 25 also indicated that for shorter duration of exposure, the force of infection was high. We see the advantage of the mathematical model as they can be used to explore changes such as factors as well as identify the type of data that needs to be collected and parameters that need to be accessed.

We comprehensive the model to describe heterogeneity in sharing frequency, andmixing between population subgroups with different risk behavior. This type of model can be developed further by increasing the number of subgroups in the model. Finally, we discussed an extension of the model by including the time since starting injecting as an additional model variable. Knowledge obtained from the mathematical model shows that, risk groups i.e. the individuals sharing injecting materials must be taken into account in data collection. The duration of exposure i.e. (difference between age at first injection and the age at test of HCV) must also been taken into account in a data collection. Based on the statistical assessment, we observe a better fit in early exposure times, mainly due to the limited amount of individuals with a longer duration of injection. So, we concluded that mathematical model does not support stochastic model.

8. Conclusion:

From a technical point of view, changing any of the parameters or initial conditions of the models can lead to protection of the population through the reduction of the number of susceptible by immunizations, reduction of the contact rate through public health campaigns and increase of the removal rate through better medical treatment of the infected individuals. The model assumed a homogenous fixed population. Further research is to extend the mathematical models by including two subgroups assuming a heterogeneous mixing pattern in the population. The mixing pattern would be based on the rates of borrowing injecting equipment in both groups and the fraction of needles individuals borrow from within and between groups respectively. The aspect ofcoinfections with other associated disease like HIV, whose risk may be dependent on sharing of

needles or other injecting materials, could also be researched. Mathematical modeling can enable evaluating the cost associated with those different strategies and guiding optimal resource allocation.

9. References:

1. Kretzschmar M, Weiessing L (2006):Modeling the transmission of Hepatitis C in injecting drug users .In Hepatitis C and injecting drug use: impact, costs and policy options Edited by European Monitoring Center for Drugs and Drug Addiction ; 2006:143-159.
2. Dixit NM (2008): Advances in the mathematical modeling of Hepatitis C virus dynamics. Journal of the Indian Institute of Science 88(1):3743.
3. Neumann AU ,Lam, Dahari H, Gretch DR, Wiley TE, Layden TJ, Perelson AS (1998):Hepatitis viral dynamics in vivo and the antiviral efficacy of interferon –therapy .Science 282:103-107 .
4. Anderson Britton Stochastics epidemic models and their statistical analysis. NewYork: Springer 2000.
5. Kermack W, Mc Kendrick A. A contribution to the Mathematical Theory of Epidemics. Proceedings of the Royal Society of London Series A.1927; 115:700-21.