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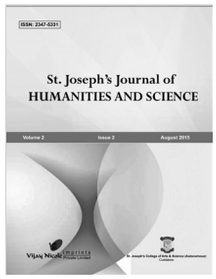

EXPECTED TIME TO SEROCONVERSION USING TWO SOURCES OF HIV TRANSMISSION – SHOCK MODEL APPROACH

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Abstract

The spread of the HIV infection has created on pandemic situation all over the world. It has become necessary to have the combined efforts of medical personnel social workers mathematicians and Statisticians to study the different aspects of this infection and its spread. One of the interesting aspects of study is to estimate the likely time at which on infected persons becomes seropositive it is in this connection the Antigenic Diversity Threshold is considered. In this paper two components namely sexual contacts and needle sharing are the modes of transmission. Numerical examples are given to illustrate various aspects of the model considered for the expected time and variance to seroconversion.

Keywords: Antigenic Diversity Threshold, Anti Retroviral Therapy, HIV Infected, Seroconversion.

INTRODUCTION

The occurrence of AIDS epidemics are amongst the forefront public health changes that the world has faced in recent past. Millions of people died of HIV infection during the last three decades. In the study of HIV infection the different modes of transmission of HIV is an interesting concept of study.

There are four different modes of transmission and they are:

1. Homo (or) Hetero sexual contacts
2. Sharing unsterile needles
3. Transmission of contaminated blood product
4. From mother to baby in the fetus

Among the four models of transmission, sexual contact is the most important mode of transmission of HIV. Sexual contacts and Needle sharing are the two source of HIV infection. The threshold of any individual is a random variable. If the total damage crosses a threshold level Y which itself is a random variable, the seroconversion occurs and a person is recognized as infection. The inter-arrival times between successive contacts, the sequence of damage and the threshold are mutually independent. Essary *et al*. (1973), consider a component, which can be either an engineering system or a bio-component, subjected to shocks occurring randomly in time.

One can see for more detail related to the study of expected time through shock model in Palanivel *et al.* (2009), threshold level using Multisource of HIV Transmission by Pandiyan *et al.* (2010). Rajivgandhi et *al.* (2010) and Ramajayam and Elangovan (2015) discussed about the expected time to cross the

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threshold level of the component. Mathematical model is obtained for the expected time of breakdown point to reach the threshold level through three parameter Weibull distribution. Numerical illustrations are provided for different combinations of the parameters in the distribution of the random variables used in this model.

Assumptions of the Models

i. A person is exposed to HIV infection. At every epoch of contact with an infected there is some contribution to the antigenic diversity.

ii. Anti Retroviral Therapy is administered to the infected.

iii. There is a particular level of antigenic diversity of the invading, and it is called the antigenic diversity threshold. If antigenic diversity crosses this threshold the seroconversion takes place.

iv. The interarrival times between the successive contacts are random variables which are identically independently distributed.

Notations

X_i: a continuous random variable denoting the amount of damage/depletion caused to the system due to the exit of persons on the i^{th} occasion of policy announcement, i=1,2,3,... k and X'_i S are i.i.d and X_i = X for all *i*.

Y_1,Y_2: continuous random variable denoting the threshold levels for the two grades which follows three parameter Weibull distribution.

g(.): The probability density functions (p.d.f) of X_i

g_k(.): The k- fold convolution of g(.) i.e., p.d.f. of $\sum_{i=1}^{k} X_i$

g*(.): Laplace transform of g(.)

g_k*(.): Laplace transform of g_k(.)

h(.): The probability density function of random threshold level which has three parameter Weibull distribution and H(.) is the corresponding Probability generating functions.

U: a continuous random variable denoting the inter-arrival times between decision epochs.

f(.) : p.d.f. of random variable U with corresponding Probability Generating function.

$V_k(t)$: $F_k(t) - F_{k+1}(t)$

$F_k(t)$:Probability that there are exactly 'k' policies decisions in (0,t)

S(.): The survivor function i.e. P(T >t)

1 – S(t) = L(t)

Model Description and Results

Any component exposed to shocks which cause damage to the immune system is likely to fail when the total cumulated damage exceed a level called threshold.

$$F(x) = 1 - e^{-\left(\frac{x-\mu}{\sigma}\right)^{\alpha}}$$

$$F(x) = \left[1 - e^{-\left(\frac{x-\mu_1}{\sigma_1}\right)^{\alpha}}\right]\left[1 - e^{-\left(\frac{x-\mu_2}{\sigma_2}\right)^{\alpha}}\right]$$

Taking α=1 we get

$$\overline{H}(x) = e^{-\left(\frac{x-\mu_1}{\sigma_1}\right)} + e^{-\left(\frac{x-\mu_2}{\sigma_2}\right)} - e^{-\left(\frac{x-\mu_1}{\sigma_1}\right)} e^{-\left(\frac{x-\mu_2}{\sigma_2}\right)}$$

In general, assuming that the threshold Y follows a three parameter Weibull distribution with parameter σ, μ it can be proved that

Transfer of system from to Y_1, Y_2 is also possible. We have the breakdown of the component is at Y = max (Y_1, Y_2).

$$P\left[\max(Y_1, Y_2)\right] = P\left[(Y_1 < Y) \cap (Y_2 < Y)\right]$$
$$= P(Y_1 < Y) \cap P(Y_2 < Y)$$

Now that Y_1 and Y_2 follow three parameter Weibull distribution with parameter σ_1, σ_2, μ_1, μ_2

$$P(X_i < Y) = \int_0^{\infty} g^*(x)\overline{H}(x)dx$$

$$= g^*\left[\left(\frac{1-\mu_1}{\sigma_1}\right)^k\right] + g^*\left[\left(\frac{1-\mu_2}{\sigma_2}\right)^k\right]$$
$$- g^*\left\{\left(\frac{1-\mu_1}{\sigma_1}\right)^k + \left(\frac{1-\mu_2}{\sigma_2}\right)^k\right\}$$

Survival analysis is a class of statistical methods for studying the occurrence and timing of events. The survival function S(t) is

P (exactly k policy decisions in (0, t)) = $F_k(t) - F_{k+1}(t)$ with $F_0(t) = 1$

It may happen that successive shocks become increasingly effective in causing damage, even though they are independent. This means that $V_k(t)$, the distribution function of the k^{th} damage is decreasing in

k = 1, 2, ... for each t. It is also known from renewal process that

$$P(T > t) = \sum_{k=0}^{\infty} V_k(t)\ P(X_i < Y)$$

$$L(t) = 1 - S(t)$$

Taking Laplace Transformation of life time L(t), We get,

$$= 1 - \left\{ \sum_{k=0}^{\infty} \left(F_k(t) - F_{k+1}(t)\right) \left[g^* \left(\frac{1-\mu_1}{\sigma_1} \right) \right]^k + \left\{ \sum_{k=0}^{\infty} \left(F_k(t) - F_{k+1}(t)\right) \left[g^* \left(\frac{1-\mu_2}{\sigma_2} \right) \right]^k \right\} \right.$$

$$\left. - \sum_{k=0}^{\infty} \left(F_k(t) - F_{k+1}(t)\right) \left[g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right) \right]^k \right\}$$

$$L^*(S) = \frac{\left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right] f^*(s)}{\left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right] f^*(s)} + \frac{\left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right] f^*(s)}{\left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right] f^*(s)} - \frac{\left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right] f^*(s)}{\left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right] f^*(s)}$$

$$= \frac{\left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right] \left(\frac{\eta}{\eta + s} \right)}{\left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right] \left(\frac{\eta}{\eta + s} \right)} + \frac{\left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right] \left(\frac{\eta}{\eta + s} \right)}{\left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right] \left(\frac{\eta}{\eta + s} \right)} - \frac{\left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right] \left(\frac{\eta}{\eta + s} \right)}{\left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right] \left(\frac{\eta}{\eta + s} \right)}$$

$$= \frac{\eta \left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right]}{\left[\eta + s - g^* \left(\frac{1-\mu_1}{\sigma_1} \right) \eta\right]} + \frac{\eta \left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right]}{\left[\eta + s - g^* \left(\frac{1-\mu_2}{\sigma_2} \right) \eta\right]} - \frac{\eta \left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right]}{\left[\eta + s - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right) \eta\right]}$$

$$E(T) = \frac{d}{ds} L^*(s) \text{ given } s = 0$$

$$E(T) = \frac{1}{\eta \left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right]} + \frac{1}{\eta \left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right]} - \frac{1}{\eta \left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right]}$$

$g^*(\cdot) \sim \exp(\mu)$,

$$g^* \left(\frac{1-\mu_1}{\sigma_1} \right) \sim \exp \left(\frac{\mu_1}{\mu_1 + \left(\frac{1-\mu_1}{\sigma_1} \right)} \right), \quad g^* \left(\frac{1-\mu_2}{\sigma_2} \right) \sim \exp \left(\frac{\mu_2}{\mu_2 + \left(\frac{1-\mu_2}{\sigma_2} \right)} \right)$$

$$g^* \left[\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right] \sim \exp \left(\frac{\mu_1 + \mu_2}{\mu_1 + \mu_2 + \left[\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right]} \right)$$

$$= \frac{1}{\eta \left[1 - g^* \left(\frac{1-\mu_1}{\sigma_1} \right)\right]} + \frac{1}{\eta \left[1 - g^* \left(\frac{1-\mu_2}{\sigma_2} \right)\right]} - \frac{1}{\eta \left[1 - g^* \left(\left(\frac{1-\mu_1}{\sigma_1} \right) + \left(\frac{1-\mu_2}{\sigma_2} \right) \right)\right]}$$

On simplification we get,

$$E(T) = \frac{\sigma_1\mu_1 + 1 - \mu_1}{\eta[1-\mu_1]} + \frac{\sigma_2\mu_2 + 1 - \mu_2}{\eta[1-\mu_2]} - \frac{\sigma_1\sigma_2\mu_1 + \sigma_1\sigma_2\mu_2 + \sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2}{\eta[\sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]}$$

$$E(T^2) = \frac{d^2}{ds^2}L^*(s) \text{ given } s = 0$$

$$E(T^2) = \frac{2[\sigma_1\mu_1 + 1 - \mu_1]^2}{\eta^2[1-\mu_1]} + \frac{2[\sigma_2\mu_2 + 1 - \mu_2]^2}{\eta^2[1-\mu_2]} - \frac{2[\sigma_1\sigma_2\mu_1 + \sigma_1\sigma_2\mu_2 + \sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2}{\eta^2[\sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2}$$

$$V(T) = E(T^2) - [E(T)]^2$$

$$V(T) = \frac{2[\sigma_1\mu_1 + 1 - \mu_1]^2}{\eta^2[1-\mu_1]} + \frac{2[\sigma_2\mu_2 + 1 - \mu_2]^2}{\eta^2[1-\mu_2]} - \frac{2[\sigma_1\sigma_2\mu_1 + \sigma_1\sigma_2\mu_2 + \sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2}{\eta^2[\sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2} - \left[\frac{\sigma_1\mu_1 + 1 - \mu_1}{\eta[1-\mu_1]} + \frac{\sigma_2\mu_2 + 1 - \mu_2}{\eta[1-\mu_2]} - \frac{\sigma_1\sigma_2\mu_1 + \sigma_1\sigma_2\mu_2 + \sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2}{\eta[\sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]}\right]^2$$

$$V(T) = \frac{[\sigma_1\mu_1 + 1 - \mu_1]^2}{\eta^2[1-\mu_1]^2} + \frac{[\sigma_2\mu_2 + 1 - \mu_2]^2}{\eta^2[1-\mu_2]^2} - \frac{[\sigma_1\sigma_2\mu_1 + \sigma_1\sigma_2\mu_2 + \sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2}{\eta^2[\sigma_2 - \sigma_2\mu_1 + \sigma_1 - \sigma_1\mu_2]^2}$$

Numerical Examples

On the basis of the numerical illustration of the following conclusions regarding expected time and variance consequent to the changes in the different parameter can be observed in fig.1 to fig.5.

Table 1: Variation in E (T) and V (T) for changes in σ_1 and

$\mu_1 = 1.75, \mu_2 = 1.0, \sigma_2 = 1.5, \eta = 0.5$

σ_1	E(T)	V(T)
1.0	3.8323	13.0934
1.2	3.7054	12.3845
1.4	2.9453	10.6253
1.6	2.0967	8.3481
1.8	1.9831	6.3271

Fig.1: Variation in E (T) and V (T) for Changes in σ_1

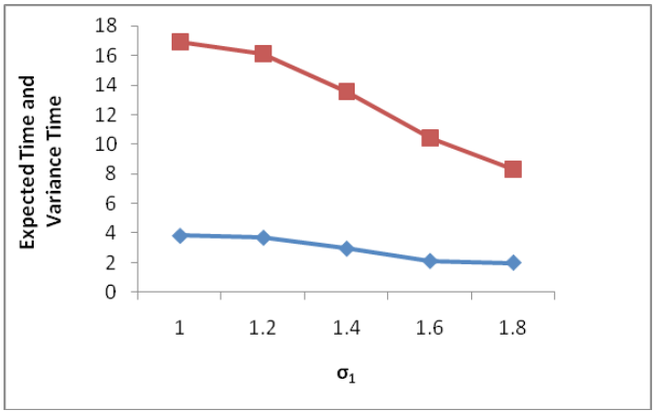

Table 2: Variation in E (T) and V (T) for changes in σ_1 and

$\mu_1 = 1.75, \mu_2 = 1.0, \sigma_2 = 1.2, \eta = 0.5$

σ_2	E(T)	V(T)
0.5	4.6752	23.0934
1.0	3.9790	22.3389
1.5	3.2453	16.7545
2.0	2.7967	14.247
2.5	1.9831	12.3621

Fig.2: Variation in E (T) and V (T) for Changes in σ_2

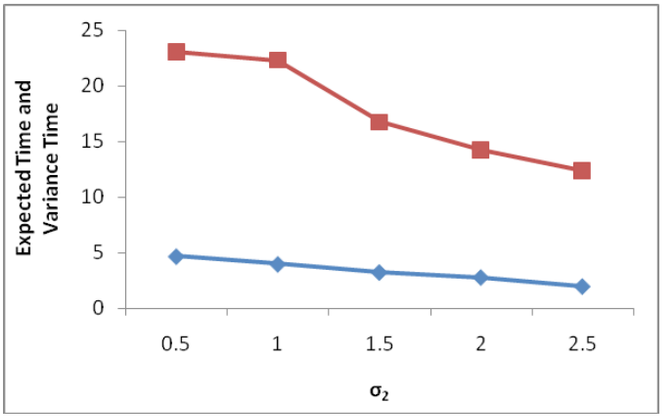

Table 3: Variation in E (T) and V (T) for changes in and μ_1

$\sigma_1 = 1.2, \mu_2 = 1.0, \sigma_2 = 1.5, \eta = 0.5$

μ_1	E(T)	V(T)
1.0	2.6210	6.3462
1. 5	2.9853	7.0920
2.0	3.8093	7.9823
2.5	4.8325	8.8250
3.0	8.3420	9.5780

Fig.3: Variation in E (T) and V (T) for Changes in μ_1

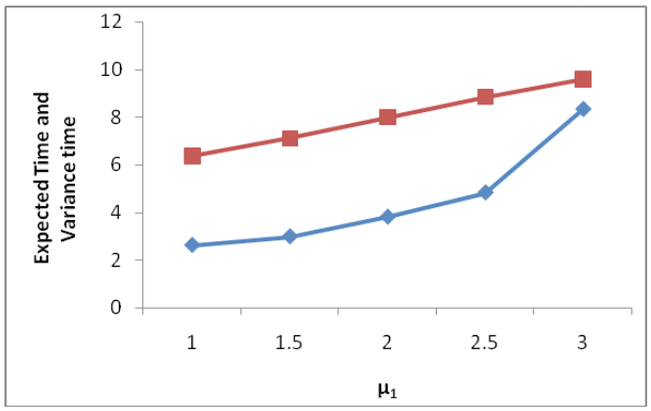

Fig.5: Variation in E (T) and V (T) for Changes in η

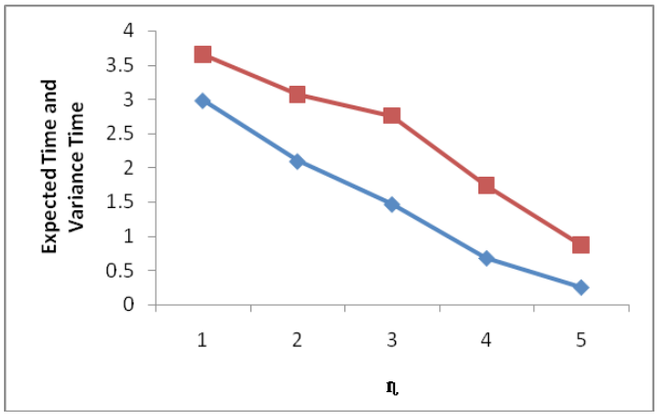

Table 4: Variation in E (T) and V (T) for changes in μ_2 and

$\mu_1 = 1.75, \sigma_1 = 1.2, \sigma_2 = 1.5, \eta = 0.5$

μ_2	*E(T)*	*V(T)*
0.2	8.3468	13.2150
0.4	9.0253	13.4357
0.6	10.3216	14.0214
0.8	10.9047	14.9830
1.0	11.2173	15.6374

Fig.4: Variation in E (T) and V (T) for Changes in μ_2

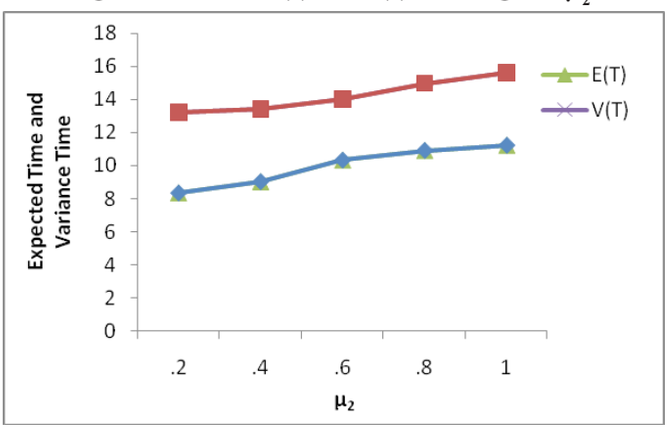

Table 5: Variation in E (T) and V (T) for changes in η and

$\mu_1 = 1.75, \mu_2 = 1.0, \sigma_2 = 1.5, \sigma_1 = 1.2$

η	*E(T)*	*V(T)*
1	2.9835	3.6589
2	2.0925	3.0725
3	1.4638	2.7610
4	0.6752	1.7458
5	0.2478	0.8735

CONCLUSION

It is observed that from table 1 and table 2 the parameter denoting the antigenic diversity threshold σ_1 and σ_2 increases and the threshold parameter μ_1, μ_2 are kept fixed, the simulated results shows that as the inter arrival time follows exponential distribution η = 0.5 take the value the expected time to cross the antigenic diversity threshold decreases and variance also decreases which is depicted in fig.1 and fig.2. This is due to fact that the antigenic diversity threshold increases expected time to cross the antigenic diversity threshold is decreases.

From table 3 and table 4 it is observed that the threshold parameter μ_1 and μ_2 and the parameter of the antigenic diversity threshold σ_1 and σ_2 are kept fixed, the simulated results shows that as the inter arrival time follows exponential distribution η = 0.5 take the value the expected time to cross the antigenic diversity threshold increases and variance also increases which is depicted in fig.3 and fig.4. It is value of η which is parameter of the distribution of the inter arrival times between contacts increases then the expected time and variance time also decreases, which is means that the contacts are more frequent and hence the seroconversion occurs earlier and hence both expected time and variance time decreases.

To analyze HIV/AIDS epidemiological data, many parametric distributions have been assumed for the HIV infection and seroconversion without due regard to the dynamics of the HIV epidemic and the

biological and clinical features of the HIV. Results of practical utility can be achieved by collecting real life data by assuming appropriate distributions and test for the goodness of fit can be used to validate the model. The major use of mathematical models of the transmission dynamics of HIV at present is to focus attention on the epidemiological parameters that need to be measured to predict future trends and to help to assess how different methods of control will influence the incidence of AIDS.

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