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A stochastic model for the estimation of time to seroconversion of HIV transmission using Erlang truncated exponential distribution

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Abstract
The use of stochastic model in the study of HIV infection, the estimation of the likely time at which seroconversion take place is an important aspect. The human immune system collapses very much based on the antigenic diversity of the antigen namely HIV attained in each successive contacts and it occurs leading to seroconversion. In this paper focuses on the study of stochastic model for predicting the seroconversion time of HIV transmission under the assumption that the threshold level of antigenic diversity is a random variable follows Erlang truncated exponential distribution. The mean time to seroconversion and its variance are derived and its numerical illustrations are also furnished.

Keywords: acquired immune deficiency syndrome (AIDS), human immunodeficiency virus (HIV), antigenic diversity threshold, seroconversion, cumulative damage process

1. Introduction
Mathematical and statistical model based on the under lying transmission mechanism of HIV help the social medical and scientific community to understand better how the disease spread in the community. The science of epidemiology has great implications in the applications of epidemic disease Acquired Immune Deficiency Virus (AIDS). AIDS is an infectious disease caused by retrovirus called Human Immunodeficiency Virus (HIV). The HIV can be transmitted through a variety of contact mechanisms that include homo or hetro sexual contacts, transfusion an infected needle sharing among intravenous drug abuse and mother to fetus. The per contact transmission probability is known as infectivity. Jewell and Shiboshi (1990) have obtained the expression of hazard rate and prevalence function using the available data from the partner study.

The transmission of more and more HIV from the infected person to the uninfected, the antigenic variations would be on the increase. The antigenic diversity mean the divergent of the virus with spread immune property to product theme self again the antibody which are develop to fight again the inspection. The antigenic diversity threshold which mean the antigenic diversity cross the particular level then the human immunity system collapses and seroconversion take place immediately. The antigenic diversity threshold and its estimation has been discussed by Stilianakis *et al*. (1994) [9] and Nowak May (1990).

A stochastic model for the estimation of expected time to seroconversion and its variance has been derived under different threshold distributions (Exponential, Gamma, Mixed Exponential, Exponentiated Exponential, Exponential Geometric and Exponentiated Modified Weibull distribution) by Sathiyamoorthiand Kannan (2001) [8], Kannan *et al*. (2007) [2], Kannan *et al*. (2011) [3], Kannan *et al*. (2011) [4], Kannan *et al*. (2013) [5], Kannan *et al*. (2015) [6].

In this paper, the stochastic model for the estimation of expected time to seroconversion and variance of the seroconversion time are derived under the assumption that threshold level of antigenic diversity is a random variable which follows Erlang truncated exponential distribution. In developing such a stochastic model, the shock model and cumulative damage process discussed by Esary *et al*. (1973) [7] is used. In this study the theoretical results are substantiated using numerical data simulated.

2. Assumptions of the Model

The following are the assumptions used in this model.

1. Sexual contact is the only source of HIV transmission.
2. An uninfected individual has sexual contacts with a HIV infected partner, and a random number of HIV are getting transmitted at each contact.
3. An individual is exposed to a damage process acting on the immune system and damage is assumed to be linear and cumulative.
4. The damages to individuals are caused by transmission of HIV at each contact and the interarrival times between contacts are assumed to be i.i.d. random variables.
5. The total damage caused when exceeds a threshold level *Y* which itself is a random variable, the seroconversion occurs and a person is recognized as a seropositve.
6. The process which generates the contacts and the sequence of damages to the threshold are mutually independent.

3. Notations

X_i	:	a random variable denoting the increase in the antigenic diversity arising due to the HIV transmitted during the i^{th} contact X_1, X_2, … X_k are continuous i.i.d. random variables, with p.d.f. g(.) and c.d.f. G(.).
Y	:	a random variable representing antigenic diversity threshold and follows erlang truncated exponential distribution with parameters θ and λ, the p.d.f being h(.) and c.d.f H(.).
U_i	:	a continuous random variable denoting the interarrival times between successive contacts with p.d.f.f(.) and c.d.f. F(.).
$g_k(.)$	:	The p.d.f of random variable $\sum_{i=1}^{k} X_i$.
$F_k(.)$	:	The k^{th} convolution of F (.).
T	:	A continuous random variable denoting the time of seroconversion with p.d.f. *l*(.) and c.d.f. L(.).
$V_k(t)$	:	The probability of exactly k contacts in (o, t].
$l^*(s)$	:	The Laplacestieltje'stransform of *l*(t).
$f^*(s)$	:	The Laplacestieltje'stransform of *f* (t).

4. Results

It can be shown that

$$P\left[\sum_{i=1}^{k} X_i < Y\right] = \int_0^{\infty} g_k(x)\,\bar{H}(x)\,dx \qquad \ldots (1)$$

Where $\bar{H}(x) = 1 - H(x)$

Let Y ~ Erlang truncated exponential (λ, θ)

$$\bar{H}(y) = e^{-\theta x\left(1-e^{-\lambda}\right)}$$

$$P\left(\sum_{i=1}^{k} X_i < Y\right) = \int_0^{\infty} g_k(x)\bar{H}(x)\,dx$$

$$= \int_0^{\infty} g_k(x)e^{-\theta x(1-e^{-\lambda})}\,dx$$

$$= \left[g^*(\theta(1-e^{-\lambda}))\right]^k$$

$$S(t) = P[T > t] = \sum_{k=0}^{\infty} \Pr\{\text{there are exactly k contacts in } (0,t]\} * \Pr\{\text{the cumulative total of antigenic diversity} < Y\}$$

$$\therefore S(t) = \sum_{K=0}^{\infty} V_k(t)\,P\left[\sum_{i=1}^{k} X_i < Y\right]$$

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)]\left[g^*(\theta(1-e^{-\lambda}))\right]^k$$

$$L(t) = 1 - S(t) = 1 - \left\{\sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)]\left[g^*(\theta(1-e^{-\lambda}))\right]^k\right\}$$

$$= 1 - \left\{1 - \left[1 - g^*(\theta(1 - e^{-\lambda}))\right] \sum_{k=0}^{\infty} [F_k(t)] \left[1 - g^*(\theta(1 - e^{-\lambda}))\right]\right\}^{k-1}$$

$$= \left\{\left[1 - g^*(\theta(1 - e^{-\lambda}))\right] \sum_{k=0}^{\infty} [F_k(t)] \left[1 - g^*(\theta(1 - e^{-\lambda}))\right]\right\}^{k-1}$$

Now,
Taking Laplace Stieltje's transform of *l*(t) we get,

$$l^*(s) = \frac{\left[1 - g^*(\theta(1 - e^{-\lambda}))\right] f^*(s)}{[1 - g^*(\theta(1 - e^{-\lambda}))f^*(s)]}$$

Onsimplification

Since *f*(.) follows exp (c), then

$$\text{If} \quad f^*(\mathrm{s}) = \frac{\mathrm{c}}{\mathrm{c} + \mathrm{s}}$$

Then

$$= \frac{\left[1 - g^*(\theta(1 - e^{-\lambda}))\right] \left(\frac{c}{c+s}\right)}{\left[1 - g^*(\theta(1 - e^{-\lambda})) \left(\frac{c}{c+s}\right)\right]}$$

$$= \frac{\left[1 - g^*(\theta(1 - e^{-\lambda}))\right] c}{[c + s - g^*(\theta(1 - e^{-\lambda}))c]}$$

Now,

$$\mathrm{E}(\mathrm{T}) = -\left.\frac{\mathrm{d}l^*(\mathrm{s})}{\mathrm{ds}}\right|_{s=0}$$

$$= \frac{(-1)\left[1 - g^*(\theta(1 - e^{-\lambda}))\right] c}{[c + s - g^*(\theta(1 - e^{-\lambda}))c]^2}$$

$$= \frac{1}{c[1 - g^*(\theta(1 - e^{-\lambda}))]}$$

Let g(.) follows exponential distribution with parameter μ, then

$$\mathrm{g}^*(\lambda) = \frac{\mu}{\mu + \lambda}$$

Then $E(T) = \frac{1}{c\left\{1 - \frac{\mu}{\mu+\theta} + \frac{\mu}{\mu+\theta\, e^{-\lambda}}\right\}}$

$= \frac{(\mu+\theta)(\mu+\theta\, e^{-\lambda})}{c[\mu^2+2\theta\mu+\theta^2 e^{-\lambda}]}$Onsimplification … (2)

$$\mathrm{E}(\mathrm{T}^2) = \left.\frac{\mathrm{d}^2 l*(\mathrm{s})}{\mathrm{ds}^2}\right|_{\mathrm{S}=0}$$

$$E(T^2) = \frac{2\left[1 - g^*(\theta - \theta e^{-\lambda})\right] c}{[c + s - g^*(\theta - \theta e^{-\lambda})c]^3}$$

$= \frac{2}{c^2[1-g^*(\theta-\theta e^{-\lambda})]^2}$ … (3)

Substituting g*(λ) in equation (3)

$$E(T^2) = \frac{2}{c^2\left\{1 - \frac{\mu}{\mu+\theta} + \frac{\mu}{\mu+\theta\, e^{-\lambda}}\right\}^2}$$

$$= \frac{2(\mu+\theta)^2(\mu+\theta\, e^{-\lambda})^2}{c^2[\mu^2+2\theta\mu+\theta^2 e^{-\lambda}]^2}$$

The variance of time to seroconversions

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

$$= \frac{2(\mu+\theta)^2(\mu+\theta\, e^{-\lambda})^2}{c^2[\mu^2+2\theta\mu+\theta^2 e^{-\lambda}]^2} - \frac{(\mu+\theta)^2(\mu+\theta\, e^{-\lambda})^2}{c^2[\mu^2+2\theta\mu+\theta^2 e^{-\lambda}]^2}$$

$$V(T) = \frac{(\mu+\theta)^2(\mu+\theta\, e^{-\lambda})^2}{c^2[\mu^2+2\theta\mu+\theta^2 e^{-\lambda}]^2} \quad \ldots (4)$$

5. Numerical Illustrations

Table 1

θ =0.2, λ=0.3 μ=0.5		
C	**Mean**	**Variance**
1	0.945962	0.894845
2	0.472981	0.223711
3	0.315321	0.099427
4	0.236491	0.055928
5	0.189192	0.035794
6	0.15766	0.024857
7	0.135137	0.018262
8	0.118245	0.013982
9	0.105107	0.011047
10	0.094596	0.008948

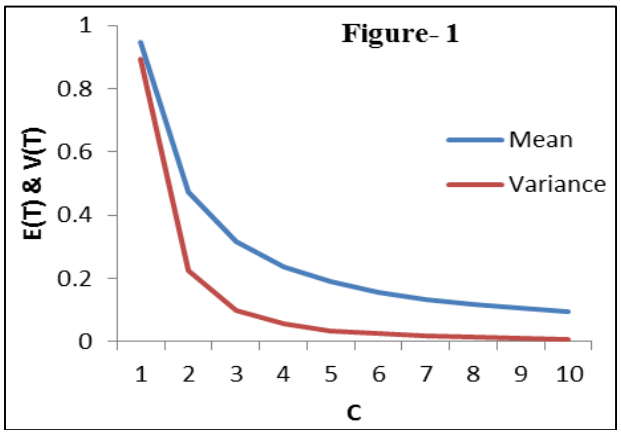


Table 2

θ =0.2, λ =0.3, c=2		
μ	**Mean**	**Variance**
0.5	0.472981	0.223711
1	0.481871	0.232199
1.5	0.486499	0.236681
2	0.489267	0.239382
2.5	0.491099	0.241178
3	0.492399	0.242457
3.5	0.493369	0.243413
4	0.494119	0.244154
4.5	0.494718	0.244746
5	0.495206	0.245229

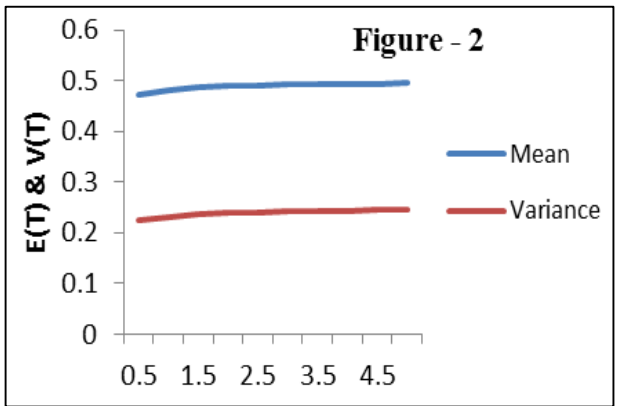


Table 3

λ =0.3, μ=0.2, c=1		
θ	Mean	Variance
0.01	0.988239	0.976616
0.02	0.978534	0.957529
0.03	0.970473	0.941818
0.04	0.963741	0.928798
0.05	0.958096	0.917949
0.06	0.953347	0.908871
0.07	0.949343	0.901253
0.08	0.945962	0.894845
0.09	0.943107	0.889451
0.1	0.940696	0.884909

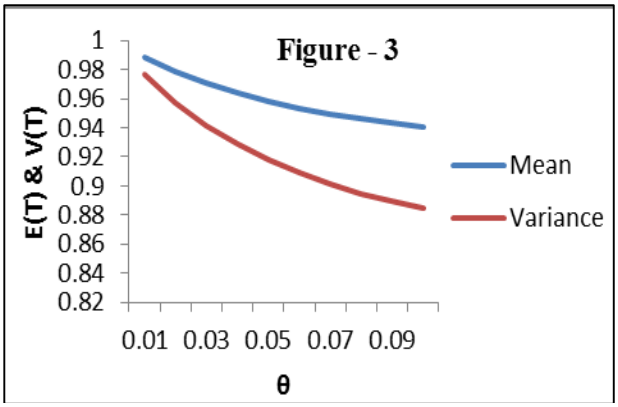
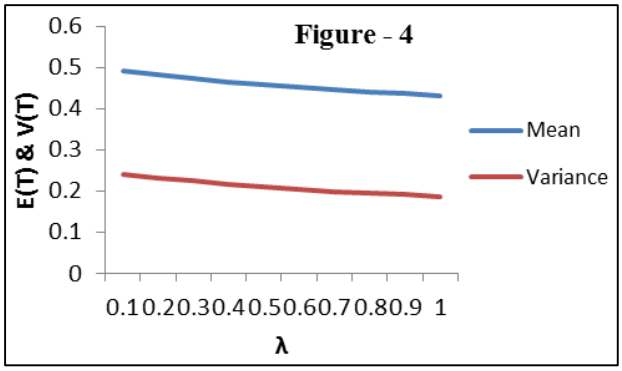


Table 4:

θ =0.2, μ=0.3, c=2		
λ	**Mean**	**Variance**
0.1	0.490214	0.240309
0.2	0.481225	0.231578
0.3	0.472981	0.223711
0.4	0.465429	0.216624
0.5	0.458518	0.210238
0.6	0.4522	0.204485
0.7	0.44643	0.199299
0.8	0.441164	0.194626
0.9	0.436363	0.190413
1	0.431988	0.186614



6. Conclusion

1. In Table 1 shows the value of expected time to seroconversion corresponding to the variation in c the parameter of the distribution of inter-arrival time when λ, θ, μ are kept fixed. As c increases, the value of $\frac{1}{c}$ decreases that means the inter-arrival time between contacts become smaller and so there is a corresponding decrease in expected time to seroconversion and also its variance. The graph is also plotted in Fig.1.
2. It is observed from the contribution to the antigenic diversity threshold parameter 'μ' which increases then expected time to seroconversion increases. This implies the fact that g (.) is the distribution of $X_{(i)}$, the magnitude of contribution to antigenic diversity. Since $E(X) = \frac{1}{\mu}$, as μ increase there is a decrease in the contribution of antigenic diversity. Hence, the expected time to seroconversion and also its variance for time to seroconversion increase.
3. From Table 3, as the value of θ is the parameter of the Erlang truncated exponential distribution of the threshold increases then expected time to seroconversion and variance of seroconversion decreases.
4. From the fixed values of θ, μ and c when threshold parameter 'λ' is allowed to increase then expected time to seroconversion and variance of seroconversion decrease as indicated in Table 4 and Figure 4.

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