# Determination of Expected Time to Seroconversion When the Antigenic Diversity Threshold Follows Order Statistic

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***Research Article***

***Abstract:*** In the study of HIV infection and consequent AIDS, the antigenic diversity is an important causative factor. A person, who has sexual contacts with an infected person, acquires more and more of HIV. This accentuates the increase in antigenic diversity of the invading antigen. When the total contribution to antigenic diversity on successive occasions of sexual contact crosses a particular level called the antigenic diversity, the seroconversion occurs. In this paper, the expected time to seroconversion and its variance are obtained under the assumption that the antigenic diversity is a random variable distributed as the $n^{th}$ order statistic. Numerical illustrations have also been provided.

**Key *W*ords:** antigenic diversity thershold; seroconversion; nth order statistic.

## Introduction:

The determination of the expected time to seroconversion is an important aspect in the study of HIV infection and its spread. When the cumulative antigenic diversity due to newly acquired HIV in successive contacts with an infected crosses a particular level called antigenic diversity threshold, the seroconversion occurs. The interarrival times between successive contacts are also random variables.

The antigenic diversity threshold is taken to be random variable, since it differs from one individual to another. The concept of antigenic diversity threshold has been discussed by Nowak and May (1991).Kannan and Sathiyamoorthi (2008) have obtained expected time for the antigenic diversity of an infected individual to cross the threshold assuming that the antigenic diversity threshold is a random variable which follows exponential distribution. Ratchager et.al (2003) have considered a stochastic model for the estimation of expected time to seroconversion using the concept of order statistics. Palanivel et.al (2011) have estimated the expected time and its variance assuming that the antigenic diversity threshold is distributed as the first order statistic. In this paper the same concept is extended to the case when the threshold is distributed as $n^{th}$ order statistic. The shock model and cumulative damage process discussed by Esary et.al (1973) has been used in this model to estimate the expected time to seroconversion.

**Assumptions of the model**

The following are the assumptions used in this model

- A person is exposed to HIV transmission at random epochs.
- There is a random amount of contribution to antigenic diversity at every epoch of exposure and transmission.
- The seroconversion occurs as and when the cumulative antigenic diversity crosses a level called the threshold which is a random variable
- The interarival times between successive contacts are i.i.d random variables.
- The random variable which denotes the random amount of contribution to cumulative antigenic diversity and the threshold are mutually independent.

**Notations:**

$X_i$ = a random variable denoting the contribution to the antigenic diversity, i =1,2… k and has p.d.f g(.) with c.d.f G(.).

Y = a random variable denoting the antigenic diversity threshold. It follows the $n^{th}$ order statistic, and has p.d.f $h_{(n)}(.)$ and c.d .f $H_{(n)}(.)$

$U_i$ = a random variable denoting the interarrival times between successive epochs of exposure and has p.d. f (.) and c.d.f F(.).

T = a random variable denoting the time to seroconversion with p.d.f $l(.)$ and c.d.f L(.)

$F_k(.)$ = k convolution of F(.)

## Results:

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

Let Y follows $n^{th}$ order statistic

$\therefore\ h_{(n)}(y) = n[H(y)]^{n-1}\, h(y)$ and Let $y \sim \exp(\theta)$

$= n\theta\left[1 - e^{-y\theta}\right]^{n-1}\ e^{-y\theta}$

$Now\ H_n(x) = \int_0^{x} h_{(n)}(y)\, dy$

$\overline{H_n(x)} = 1 - \left[1 - e^{-x\theta}\right]^n$

The probability that in k contacts during (0,t),the total antigenic diversity generated does not exceed the threshold level Y is ,

$P\left[\sum_{i=1}^{k} X_i < y\right] = \int_0^{\infty} g_k(x)\left[1 - (1 - e^{-x\theta})^n\right] dx$ (1)

$= \int_0^{\infty} g_k(x)\, n.e^{-x\theta} - n_{c_2} \int_0^{\infty} g_k(x)\, e^{-2x\theta} + \cdots (-1)^n \int_0^{\infty} g_k(x) e^{-nx\theta} dx$ (2)

$Now \quad S(t) = P[T > t]$

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)]\, P\left[\sum_{i=0}^{k} X_i < y\right]$$

Where $F_k(t) - F_{k+1}(t)$ denotes the probability of exactly k contacts during (0,t) by renewal theory.

$$= \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)]\left[n{g^*}_k(\theta)\right] - [n_{C_2}{g^*}_k(2\theta)] \ldots, (-1)^n {g^*}_k(n\theta)$$

$$= n[1 - g^*(\theta)] \sum_{k=1}^{\infty} F_k(t)[g^*(\theta)]^{k-1} + n_{c_2}[1 - g^*(2\theta)] \sum_{k=1}^{\infty} F_k(t)[g^*(2\theta)]^{k-1}$$

$$\ldots (-1)^n [1 - g^*(n\theta)] \textstyle\sum_{k=1}^{\infty} F_k(t)[g^*(n\theta)]^{k-1}$$ (3)

On simplication

L (t) = P [T < t] = 1- S (t) (4)

Taking the Laplace trance form of L (t) we have $L^*(s)$ and then using the relationship

$L^*(s) = \frac{1}{s}\, l^*(s)\ and\ {F_k}^*(s) = \frac{[f^*(s)]^k}{s}$

We have

Now $l^*(s) = n[1 - g^*(\theta)]f^*(s)$

$$\sum_{k=1}^{\infty} f^*(s)^{k-1}[g^*(\theta)]^{k-1}$$

$$-n_{c_2}[1 - g^*(2\theta)]f^*(s) \sum_{k=1}^{\infty} f^*(s)^{k-1}(t)[g^*(2\theta)]^{k-1}$$

$$+ \cdots (-1)^n [1 - g^*(n\theta)]f^*(s) \sum_{k=1}^{\infty} f^*(s)^{k-1}(t)[g^*(n\theta)]^{k-1}$$

$$= \frac{n[1 - g^*(\theta)]f^*(s)}{[1 - g^*(\theta)f^*(s)]} - n_{c_2} \frac{[1 - g^*(2\theta)]f^*(s)}{[1 - g^*(2\theta)f^*(s)]} + \cdots \frac{(-1)^n [1 - g^*(n\theta)]f^*(s)}{[1 - g^*(n\theta)f^*(s)]}$$ (5)

On Simplification

Then

$$T_1 = \frac{n[1-g^*(\theta)]f^*(s)}{[1-g^*(\theta)f^*(s)]}, T_2 = n_{c_2}\frac{[1-g^*(2\theta)]f^*(s)}{[1-g^*(2\theta)f^*(s)]} \ldots T_n = \frac{(-1)^n[1-g^*(n\theta)]f^*(s)}{[1-g^*(n\theta)f^*(s)]}$$

$$Now\ when\ E(T) = -\left.\frac{dl^*(s)}{ds}\right|_{s=0}$$

Assuming that g (.) ~ exp (λ) and f(.) ~ exp (μ)

$$= \frac{n(\lambda+\theta)}{(\theta\mu)} - n_{c_2}\frac{(\lambda+2\theta)}{(2\mu\theta)} + n_{c_3}\frac{(\lambda+3\theta)}{(3\mu\theta)} - n_{c_4}\frac{(\lambda+4\theta)}{(4\mu\theta)} + n_{c_5}\frac{(\lambda+5\theta)}{(5\mu\theta)} \ldots, (-1)^{n+1}\frac{(\lambda+n\theta)}{(n\theta\mu)}$$

$$\mathbf{E(T)} = \frac{n(\lambda+\theta)}{(\theta\mu)} - n_{c_2}\frac{(\lambda+2\theta)}{(2\mu\theta)} + n_{c_3}\frac{(\lambda+3\theta)}{(3\mu\theta)} - n_{c_4}\frac{(\lambda+4\theta)}{(4\mu\theta)} + n_{c_5}\frac{(\lambda+5\theta)}{(5\mu\theta)} \ldots, (-1)^{n+1}\frac{(\lambda+n\theta)}{(n\theta\mu)} \quad (6)$$

Now to find E ($T^2$) we have

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

Now taking the terms $T_1, T_2, T_3, \ldots T_n$ we have

$$\left.\frac{d^2{T_1}^2(s)}{ds^2}\right|_{s=0} = \frac{2n(\lambda+\theta)^2}{(\theta\mu)^2}$$

$$\left.\frac{d^2{T_n}^2(s)}{ds^2}\right|_{s=0} = \frac{(-1)^{n+1}(\lambda+n\theta)^2}{(n\mu\theta)^2}$$

$$= \frac{2n(\lambda+\theta)^2}{(\theta\mu)^2} - -n_{c_2}\frac{(\lambda+2\theta)^2}{2(\mu\theta)^2} + \cdots \frac{(-1)^{n+1}(\lambda+n\theta)^2}{(n\mu\theta)^2} \quad (7)$$

∴ Now $V(T) = E(T^2) - [E(T)]^2$

From (6) and (7) the expression for V (T) can be obtained.

$$V(T) = \left\{\frac{2n(\lambda+\theta)^2}{(\theta\mu)^2} - -n_{c_2}\frac{(\lambda+2\theta)^2}{2(\mu\theta)^2} + \cdots \frac{(-1)^{n+1}(\lambda+n\theta)^2}{(n\mu\theta)^2}\right\} - \left[\frac{n(\lambda+\theta)}{(\theta\mu)} - n_{c_2}\frac{(\lambda+2\theta)}{(2\mu\theta)} + n_{c_3}\frac{(\lambda+3\theta)}{(3\mu\theta)} - n_{c_4}\frac{(\lambda+4\theta)}{(4\mu\theta)} + n_{c_5}\frac{(\lambda+5\theta)}{(5\mu\theta)} \ldots, (-1)^{n+1}\frac{(\lambda+n\theta)}{(n\theta\mu)}\right]^2 \quad (8)$$

## Conclusions:

- When λ which is the parameter of the random variable $X_i$, denoting the magnitude of contribution to antigenic diversity is on the increase, it is seen that E (T) increases. This is due to the fact that $X_i$ follows exponential distribution and so E ($X_i$) = 1/λ. As λ increases then, 1/λ which is the contribution to antigenic diversity decreases. Hence it takes more time to cross the threshold. This is true when Y follows $n^{th}$ order statistic also. This has been shown in table (1) and figure (1).
- The inter arrival times between successive contacts distributed as exponential with parameter μ. As μ increases, then E (U) = 1/μ decreases. Hence, the contacts will be more frequent and a greater contribution to the antigenic diversity. So, it takes less time to cross the threshold. Hence E (T) becomes smaller. This has been indicated in table (2) and figure (2).
- The threshold is a random variable which is the $n^{th}$ order statistic. Now the threshold Y follows exponential with parameter θ. Hence E (y) = 1/θ and it decreases as θ increases. Hence the threshold is smaller as θ increases. So as θ increases, it takes less time to cross the threshold as indicated in table (3) and figure (3).
- As 'n' increases, then the $n^{th}$ order also increases. This would mean that the magnitude of the $n^{th}$ order statistic will be greater. Hence, the threshold is higher and so it takes more time to cross the threshold and so E (T) is on the increase. This has been indicated in table (4) and figure (4).

**Table 1**

| θ=1.5 | λ=1.2 | n=10 |
|---|---|---|
| μ | E (T) | V(T) |
| 1 | 1.08 | 1.166 |
| 2 | 0.54 | 0.291 |
| 3 | 0.36 | 0.129 |
| 4 | 0.27 | 0.072 |
| 5 | 0.21 | 0.046 |
| 6 | 0.18 | 0.032 |
| 7 | 0.15 | 0.023 |
| 8 | 0.13 | 0.018 |
| 9 | 0.12 | 0.014 |
| 10 | 0.10 | 0.011 |

**Fig 1**

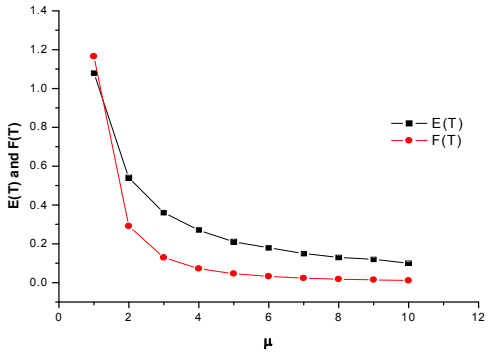



**Table 2**

| θ=1.5 | μ=1.0 | n=10 |
|---|---|---|
| λ | E (T) | V(T) |
| 1 | 0.533 | 0.284 |
| 2 | 0.567 | 0.321 |
| 3 | 0.600 | 0.360 |
| 4 | 0.633 | 0.401 |
| 5 | 0.667 | 0.444 |
| 6 | 0.700 | 0.490 |
| 7 | 0.733 | 0.538 |
| 8 | 0.767 | 0.588 |
| 9 | 0.800 | 0.640 |
| 10 | 0.833 | 0.694 |

**Fig 2**

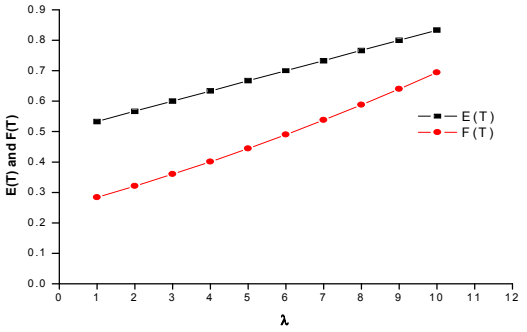



**Table 3**

| λ=1.2 | μ=1.0 | n=10 |
|---|---|---|
| Θ | E (T) | V(T) |
| 1 | 0.560 | 0.314 |
| 2 | 0.530 | 0.281 |
| 3 | 0.520 | 0.270 |
| 4 | 0.515 | 0.265 |
| 5 | 0.512 | 0.262 |
| 6 | 0.510 | 0.260 |
| 7 | 0.509 | 0.259 |
| 8 | 0.508 | 0.258 |
| 9 | 0.507 | 0.257 |
| 10 | 0.506 | 0.256 |

**Fig 3**

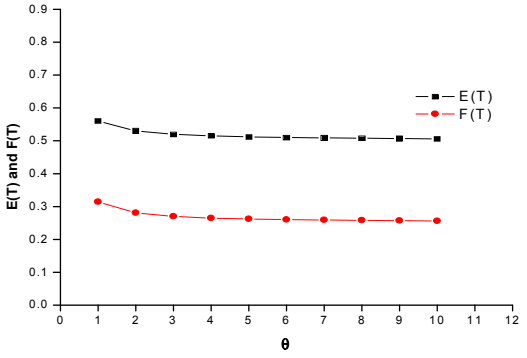
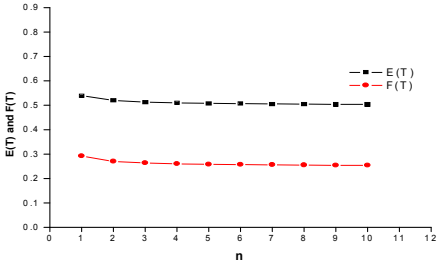



**Table 4**

| θ=1.5 | μ=1.0 | λ=1.2 |
|---|---|---|
| n | E (T) | V(T) |
| 1 | 0.540 | 0.292 |
| 2 | 0.520 | 0.270 |
| 3 | 0.513 | 0.264 |
| 4 | 0.510 | 0.260 |
| 5 | 0.508 | 0.258 |
| 6 | 0.507 | 0.257 |
| 7 | 0.506 | 0.256 |
| 8 | 0.505 | 0.255 |
| 9 | 0.504 | 0.254 |
| 10 | 0.504 | 0.254 |

**Fig 4**



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