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Tracing the CD4 count of HIV survival patient with platelet count, prothrombin time and activated partial thromboplastin time through shock model approach

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Abstract
Any component exposed to shocks which cause damage to the component is likely to fail when the total cumulated damage exceed a level called threshold. When the immune system does not accumulate the increase in shock which is the inter-arrival time, the expected life time of the human system will reach the threshold. CD4 counts are observed with three variables of time, namely Platelet Count, Prothrombin Time and Activated Partial Thromboplastin Time. Through shock model the CD4 count is being studied and the data collected in Pondicherry region is been fitted for the time to break down of the infected person.

Keywords: Threshold, Expected time, Prothrombin Time, Thromboplastin Time.

1. Introduction
It has been widely recognized that the amount of people infected with human immunodeficiency virus has been increasing in recent years, especially in developing countries. Thus, there is an urgent need for rapid diagnosis, monitoring and antiretroviral therapy. A common weakness of the statistical models is that very often the dynamics of the HIV epidemic and many important epidemiological, biological and clinical features of the HIV epidemic that are known have been ignored. The advantages from both stochastic models and statistical models are efficiently to estimate the unknown parameters and the numbers of infected people and AIDS cases to be found. The CD4 count is used to measure immune status and HIV disease progression. For more detail about the expected time to cross the threshold level one can see, Esary *et al*., (1973), R. Sathiyamoorthi (1980), C. Subramanian *et al*., (2012).
The Cumulative density function (CDF) of the Modified Weibull Distribution (MWD) $(x;\alpha,\beta,\gamma)$

$$F(x;\alpha,\beta,\gamma) = 1 - e^{-\alpha x - \beta x^{\gamma}}, \qquad x > 0$$

Ammar Sarhan and Mazen Zaindin, (2009). It is observed that the MWD can have constant, increasing and decreasing hazard rate functions which are desirable for data analysis purposes. Application on set of real data showed that the MWD can be used rather than other known distribution.
Two sources of contact with HIV transmission, an uninfected individual have sexual contacts with an HIV infected partner, a random number of HIV are getting transmitted at each contact. An individual is expressed in a damage process acting on the immune system and damage is assumed to be linear and cumulative. The damages to individual are caused by transmission of HIV at each contact and the inter arrival times between contacts are assumed to be i.i.d random variable. The total damage caused when exceeds a threshold level Y which itself is a random variable. The process which generates the contacts and the sequence of damage to the threshold are mutually independent.

2. 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, $i = 1,2,3, \ldots k$ 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 Modified 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 Modified 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 Density 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. $P(T > t)$; $1 - S(t) = L(t)$

3. Model Descriptions

The corresponding survival function of Modified Weibull distribution

$$\bar{H}(x) = e^{-(\alpha_2 x + \beta_2 x)} + e^{-(\alpha_1 x + \beta_1 x)} - e^{-(\alpha_1 x + \beta_1 x)(\alpha_2 x + \beta_2 x)} \quad (1)$$

$$P[Max(Y_1, Y_2)] = P[Y_1 < Y \cap Y_2 < Y]$$

$$= P[Y_1 < Y]P[Y_2 < Y] \quad (2)$$

One is interested in an item for which there is a significant individual variation in ability to withstand shocks. There may be no practical way to inspect an individual item to determine its threshold y. In this case, the threshold must be a random variable. The shock survival probability are given by

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

$$= [g^*(\alpha_2 + \beta_2)]^k + [g^*(\alpha_1 + \beta_1)]^k + [g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]^k \quad (3)$$

The survival function which gives the probability that the cumulative threshold will fail only after time t. $S(t) = P(T > t)$, Probability that the total damage survives beyond *t*.

It is also known from renewal process that

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

$$P(T > t) = \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)]\, [g^*(\alpha_2 + \beta_2)]^k + [g^*(\alpha_1 + \beta_1)]^k$$

$$+ [g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]^k \quad (4)$$

$$= 1 - [1 - g^*(\alpha_2 + \beta_2)] \sum_{k=1}^{\infty} F_k(t)\, [g^*(\alpha_2 + \beta_2)]^{k-1} + [1 - g^*(\alpha_1 + \beta_1)] \sum_{k=1}^{\infty} F_k(t)\, [g^*(\alpha_1 + \beta_1)]^{k-1}$$

$$+ [1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)] \sum_{k=1}^{\infty} F_k(t)\, [g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]^{k-1} \quad (5)$$

Data that measure "the length of time" until the occurrence of an event are called lifetimes, failure times or survival data. $L(T) = 1 - S(t)$. Taking Laplace transform of $L(T)$, we get

$$L(T) = 1 - \left\{1 - [1 - g^*(\alpha_2 + \beta_2)] \sum_{k=1}^{\infty} F_k(t)\,[g^*(\alpha_2 + \beta_2)]^{k-1} + [1 - g^*(\alpha_1 + \beta_1)] \sum_{k=1}^{\infty} F_k(t)\,[g^*(\alpha_1 + \beta_1)]^{k-1} + [1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)] \sum_{k=1}^{\infty} F_k(t)\,[g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]^{k-1}\right\} \quad (6)$$

Let the random variable U denoting inter arrival time, which follows an exponential with parameter. Now, $f^*(s) = \left(\frac{c}{c+s}\right)$, substituting in the below equation (7) we get,

$$L^*(s) = \frac{[1 - g^*(\alpha_2 + \beta_2)]\, f^*(s)}{[1 - g^*(\alpha_2 + \beta_2)\, f^*(s)]} + \frac{[1 - g^*(\alpha_1 + \beta_1)]\, f^*(s)}{[1 - g^*(\alpha_1 + \beta_1)\, f^*(s)]} - \frac{[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]\, f^*(s)}{[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2) f^*(s)]} \quad (7)$$

$$= \frac{[1 - g^*(\alpha_2 + \beta_2)]\, \frac{c}{c+s}}{\left[1 - g^*(\alpha_2 + \beta_2)\, \frac{c}{c+s}\right]} + \frac{[1 - g^*(\alpha_1 + \beta_1)]\, \frac{c}{c+s}}{\left[1 - g^*(\alpha_1 + \beta_1)\, \frac{c}{c+s}\right]} - \frac{[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]\, \frac{c}{c+s}}{\left[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)\, \frac{c}{c+s}\right]}$$

On simplifications we get,

$$= \frac{c\,[1 - g^*(\alpha_2 + \beta_2)]}{[c + s - g^*(\alpha_2 + \beta_2)\, c]} + \frac{c\,[1 - g^*(\alpha_1 + \beta_1)]}{[c + s - g^*(\alpha_1 + \beta_1)\, c]} - \frac{c\,[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]}{[c + s - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)\, c]} \quad (8)$$

$$E(T) = -\frac{d}{ds}\; l^*(s) \;\; given\; s = 0$$

$$= \frac{1}{c\,[1 - g^*(\alpha_2 + \beta_2)]} + \frac{1}{c\,[1 - g^*(\alpha_1 + \beta_1)]} - \frac{1}{c\,[1 - g^*(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)]} \quad on\; simplification \quad (9)$$

The inter-arrival time of the threshold follows an exponential distribution. The Laplace transformation of the exponential is given by $\frac{\mu}{\mu+\lambda}$

$$g^*(.) \sim \exp(\mu), \qquad g^*(\lambda) \sim \exp\left(\frac{\mu}{\mu + (\alpha_1 + \beta_1)}\right) \quad g^*(\lambda) \exp\left(\frac{\mu}{\mu + (\alpha_2 + \beta_2)}\right)$$

$$= \frac{1}{c\left[1 - \frac{\mu}{\mu + (\alpha_2 + \beta_2)}\right]} + \frac{1}{c\left[1 - \frac{\mu}{\mu + (\alpha_1 + \beta_1)}\right]} - \frac{1}{c\left[1 - \frac{\mu}{\mu + (\alpha_2 + \beta_2)(\alpha_1 + \beta_1)}\right]}$$

$$E(T) = \left[\frac{\mu + (\alpha_2 + \beta_2)}{c(\alpha_2 + \beta_2)} + \frac{\mu + (\alpha_1 + \beta_1)}{c(\alpha_1 + \beta_1)} + \frac{\mu + (\alpha_2 + \beta_2)(\alpha_1 + \beta_1)}{c[(\alpha_2 + \beta_2)(\alpha_1 + \beta_1)]}\right] \quad (10)$$

Data Observed of the infected person

C = Time interval of CD4 count
μ = Platelet count
β = Activated Partial Thromboplastin Time
α = Prothrombin Time

Table 1: Expected Time

c	μ	β	α
399	225	22.1	15.5
806	190	20.4	15
614	251	55.1	25.8
926	229	65.3	26.9
156	212	22.3	21.5
484	360	61.8	30.5
261	254	20.5	15.6
418	187	17.7	14.9
226	205	18.8	15.3
355	158	20.4	14.1
514	278	18.9	12.6
91	119	29.7	12.4
295	221	22	12.9
478	219	112.3	23.8
297	213	21.5	13.3
590	195	21.7	14.1
550	452	19.9	15
355	219	18.5	13.6
316	150	23	12.2
334	186	18.6	15.1

4. Conclusion

Among the 20 observed HIV positive patients, 11 were Male and 9 were Female with age group ranging from 22 to 50. Observing the CD4 counts the three variables, Platelet Count, Prothrombin Time and Activated Partial Thromboplastin Time is observed that the time to reach threshold level is very near once the CD4 counts decreases. Once the CD4 counts decrease we notice that other cells count also decreases. The possible explanation is that as the HIV infection progressed, which is characterized by reduction in CD4 count cells. The person infected with HIV is more quickly to cross the threshold level. The model shows that once the person is infected the breakdown of the immune system starts. By proper medical advice and through regular treatment the life span can be extended.

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