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Estimating the Survival Function of HIV/AIDS Patients Using Weibull Model

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Abstract

Many people are not aware of the dreadful nature of Human Immune-deficiency Virus (HIV) and Acquired Immune-Deficiency Syndrome (AIDS) and those who are aware do not know its dynamism and some other latent facts about the disease. In view of the foregoing there is need to really provide hidden facts about the dynamics and probabilities of spread of the disease to reduce its spread to the barest minimum. In this paper we shall obtain the survival function of the disease using Weibull model. This work provides information on the survival times of a cohort of infected individuals. The mean survival time was obtained as 22.579months from the resultant estimate of the shape parameter γ=1.156 and scale parameter λ=0.0256 from Weibull 7⁺⁺ simulation of n = 500. Confidence intervals were also obtained for the two parameters at $\propto$= 0.05 and it was found that the estimates are highly reliable.

Key words: Cohort, Survival time, Shape parameter, Scale parameter, Weibull7^{++}, Simulation, Confidence intervals.

INTRODUCTION

Most of the available epidemiological data indicate that the extensive spread of HIV started in sub – Sahara Africa in the late 1970s. HIV was identified independently in 1983 – 84 by Luc Montagnier, a US and French scientist (Barre-Sinoussi *et al*., 1983, Inaba and Nishiura; 2008).By the early 1980s, HIV was found a geographic band stretching from West Africa across to the Indian Ocean. The countries north of the Sahara and those in the Southern cone of the continent remained apparently untouched. By 1987, the epidemic began gradually to the south. Some of the most explosive epidemics have been seen in Southern Africa. South Africa has the largest number of people living with HIV/AIDS in the world, of about 5 million (UNAIDS, 2002, Inaba H;2008). West Africa has been relatively less affected by HIV infection than other regions of Sub- Saharan Africa. In one study of prostitutes diagnosed with Sexually Transmitted Disease (STD), the median incubation period was as short as 34 months (Anzala, et al., 1991). A second group of diseases are caused by HTLV- 1 (Human Tcell lymphotropic virus type I), the first human retrovirus to be identified. These viruses are present throughout Africa and their prevalence is highly correlated with the prevalence of HIV (Verdier et al., 1994, Heijmans H. J. A. M; 1986, HAART; 1996, Hunter, S.S 1990.).

There have been several campaigns by international organizations, and international agencies like United States Agency for International Development (USAID), World Health Organization (WHO), Society for Family Health (SFH) and local organizations like National Agency for the Control of Aids(NACA) and State Agency for the Control of AIDS(SACA), to create awareness about the deadly and incurable nature of HIV/AIDS. Despite all the efforts of the government as well as those national and international organizations to reduce its spread, it has been reported that the scourge is still on the increase. More than half of the populace in Nigeria is not aware of the dreadful nature of the disease and those who are aware do not know its dynamism and some other latent facts about the disease. In view of the foregoing there is need to really provide hidden facts about the dynamics and probabilities of spread of the disease to reduce its spread to the barest minimum. In this paper we shall obtain the survival function of the disease using Weibull model.

Survival Functions

One of the key concepts underlying the modeling HIV survival is the concept of a survival function. The survival function S (t), can be defined as the number of individuals surviving to time t, where t is the number of years since HIV infection.

A number of different distribution forms for the survival function can be used. Some of the most commonly used ones are (i) Weibull assumption (parameters λ and γ) given by $S(t) = e^{-\lambda t^{\gamma}}$ (ii) Exponential assumption (with parameter λ), $S(t) = e^{-\lambda t}$ (iii) Gompertz assumption (parameters B and C) $S(t) = e^{-\frac{B(Ct-1)}{lnC}}$ and (iv) Gamma assumption (parameters α and λ) $S(t) = 1 - \frac{\lambda^{\alpha}}{\Gamma(\alpha)}\int_0^t x^{\alpha-1}e^{-\lambda x}$

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We use Weibull assumption in this work and in particular, if we set γ = 1 in the Weibull assumption we will obtain the survival function for exponential assumption.

An alternative parameterization of the Weibull distribution which is more commonly used is one involving the median m (the time to which half of the infected individuals survive) which is given by

$$S(t) = \frac{1}{2}^{\left(\frac{t}{m}\right)^{\gamma}} \quad \text{so that} \quad m = \left(\frac{1}{\lambda} In\ 2\right)^{1/\gamma}$$

The parameter γ is called the shape parameter and it determines the variance of the time to death of infected persons i.e. it affects how concentrated the distribution of survival times is around the average time to death. A commonly used shape parameter in modeling HIV survival is 2.5 (Gregson et al 1998).

When the shape parameter γ is set to 1, the mortality or hazard rate is constant, but if γ is greater than 1, mortality rate (hazard rate increases as the duration of infection increases).

The mean and variance of Weibull survival function is given by

Mean = $E(t) = \int_0^{\infty} t\lambda\gamma t^{\gamma-1}\ \ell^{-\lambda t^{\gamma}}\ dt$ ……………………………….(1)

$$= \lambda\gamma \int_0^{\infty} t^{\gamma}\ \ell^{-\lambda t^{\gamma}}\ dt$$

If we let $K = \lambda t^{\gamma}, then$

$$\hat{\mu} = \hat{\lambda}^{-1/\hat{\gamma}}\ \Gamma\left(1 + 1/\hat{\gamma}\right) \quad \text{……………………………………….. (2)}$$

$$E(t^2) = \int_0^{\infty} \lambda\gamma t^2 t^{\gamma-1}\ \ell^{-\lambda t^{\gamma}}\ dt$$

$$= \lambda\gamma \int_0^{\infty} t^{\gamma+1}\ \ell^{-\lambda t^{\gamma}}\ dt$$

$$again\, let\ K = \lambda t^{\gamma}$$

$$= \left(\frac{K}{\lambda}\right)^{1/\gamma}$$

$$dt = \frac{1}{\lambda\gamma}\left(\frac{K}{\lambda}\right)^{1/\gamma - 1}\ dk$$

$$E(t^2) = \lambda\gamma \int_0^{\infty} \frac{1}{\lambda\gamma}\left(\frac{K}{\lambda}\right)^{1/\gamma(\gamma+1)}\left(\frac{K}{\lambda}\right)^{1/\gamma - 1} \ell^{-K}\ dk$$

$$= \int_0^{\infty} \left(\frac{K}{\lambda}\right)^{2/\gamma} \ell^{-K}\ dk$$

$$= \lambda^{-2/\gamma}\ \Gamma\left(1 + 2/\gamma\right)$$

. . .

It is worthy to note that for a Weibull distribution

$$E(t^n) = \lambda^{-n/\gamma}\ \Gamma\left(1 + n/\gamma\right) \quad (3)$$

$$\hat{\sigma}^2(t) = \lambda^{-2/\gamma}\ \Gamma\left(1 + 2/\gamma\right) - \left[\lambda^{-1/\gamma}\ \Gamma\left(1 + 1/\gamma\right)\right]^2$$

$$= \hat{\lambda}^{-2/\gamma}\left[\Gamma\left(1+2/\hat{\gamma}\right)-\left(\Gamma\left(1+1/\hat{\gamma}\right)^2\right)\right]$$ …………..(5)

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Hazard Rate Function

The hazard rate or ratio *h(t)*, usually obtained from the survival function is defined as the probability that an individual who is under observation at a time has an event at time *t*. It represents the instantaneous event rate for an individual who has already survived to time t.
The hazard rate is obtained as shown below

$$h(t) = \frac{\frac{-d}{d(t)}S(t)}{S(t)}$$ …………..(6)

Hazard Rate Of Weibull Survival Function

The survival function for Weibull distribution is given by

$$S(t) = P\,(T \geq t) \qquad \int_t^\infty \lambda\gamma t^{\gamma-1}\,\ell^{-\lambda t\gamma}\,dt \qquad = \ell^{-\lambda t\gamma}$$ ……..(7)

Hence the hazard rate function is

$$h(t) = \frac{\frac{-d}{d(t)}\ell^{-\lambda t^{\gamma}}}{\ell - \lambda t^{\gamma}} \qquad = \lambda\gamma t^{\gamma-1}$$ …………...(8)

The hazard rate of exponential survival function is constant. This explains why the weibull assumption is a better choice because the hazard rate of an infectious disease like HIV/AIDS cannot be a constant. It increases as period number of infectiousness increases.

The Median And Other Percentile Of Weibull/ Exponential Survival Function

Estimate of the median value and other percentile of a weibull distribution are obtained from the estimated survival function $\hat{S}(t)$. For the probability P, the corresponding P- level percentile (t_P) is estimated by solving the following relationship $S(\hat{t}_P) = 1 - P$

$S(\hat{t}_P) = \ell^{-\hat{\lambda}\hat{t}_P^{\gamma}}$, Hence

$$In\ \ell^{-\hat{\lambda}\hat{t}_P^{\gamma}} = In\ (1-P)$$

$$\hat{t}_P^{\gamma} = -\frac{In\ (1-P)}{\hat{\lambda}}$$

$$\hat{t}_P = \left[-\frac{In\ (1-P)}{\hat{\lambda}}\right]^{1/\gamma}$$

This expression is called the inverse weibull survival function. Thus when P = 0.5 we have the median survival time i.e the 50th percentile

$$\ell^{-\lambda\hat{t}_P} = 1 - P$$

$$\hat{\lambda}\hat{t}_P = -\ In\ (1-P)$$

$$\hat{t}_P = \left[-\frac{In\ (1-P)}{\hat{\lambda}}\right]^{1/\gamma}$$ …………………….(9)

Similarly for exponential survival function

$$\ell^{-\hat{\lambda}\hat{t}_p} = 1 - P$$

$$\hat{\lambda}\hat{t}_P = - \ In\,(1 - P)$$

$$\hat{t}_P = -\frac{In\,(1 - P)}{\hat{\lambda}} \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(10)$$

The following graphs show the survival function and the hazard rate functions for different values of parameters for Weibull and survival functions.

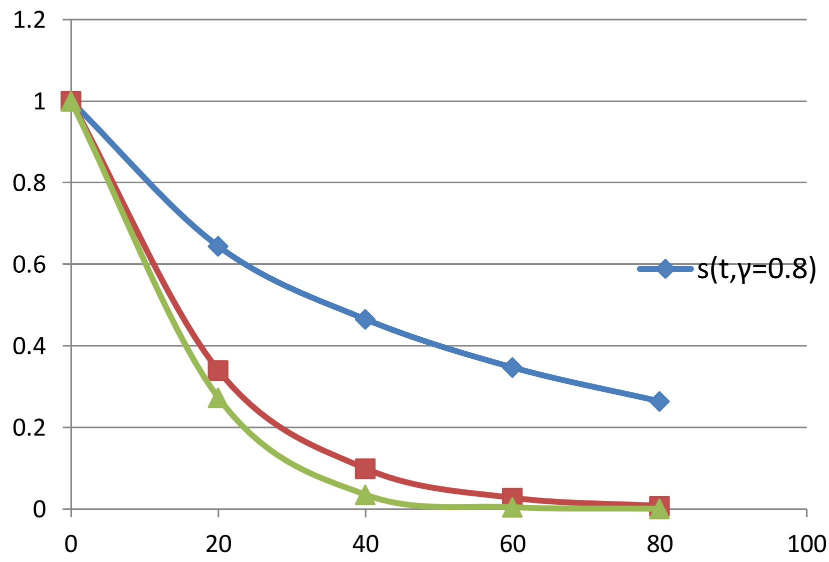

Figure 1:The Survival Function At Different Values Of The Shape Parameter γ (0.8, 1.1 and 1.2)

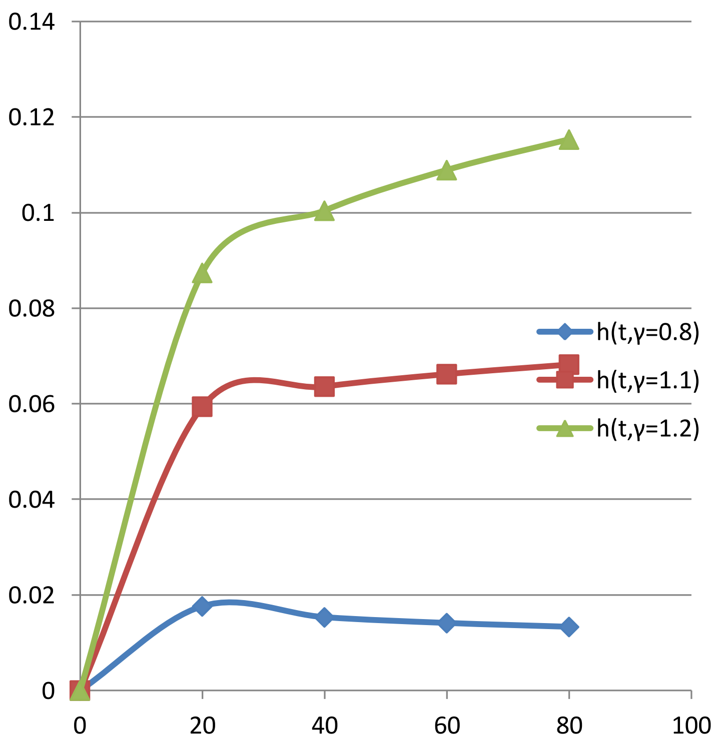

Figure 2: The Hazard Rate Function At Different Values Of The Shape Parameter **γ (0.8, 1.1 AND 1.2)**

RESULTS AND DISCUSSION

This section presents the detailed analysis of the data collected. Weibull survival functions were used and all the parameters estimated. From the AIDS data in Nigeria the total number of infected individuals in 15 – 49 years is 271400 and the total population is 4,090,000. A

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Weibull 7++ simulated survival data of n = 500 used in the work, generated the maximum likelihood estimate of the Weibull parameters and their associated variances below:
$\hat{\lambda}$ = 0.0256 and $V(\hat{\lambda})$ = 0.000044;
$\hat{\gamma}$ = 1.156 with $V(\hat{\gamma})$ = 0.00519

The associated variance of the log estimate of λ is given as

$$Var\ (\log(\hat{\lambda})) = \frac{1}{\hat{\lambda}^2} Var(\hat{\lambda})$$

and the variance of the log estimate of $\hat{\gamma}$ as

$$Var\ (\log(\hat{\gamma})) = \frac{1}{\hat{\gamma}^2} Var(\hat{\gamma}$$

An approximate 95% confidence interval based on the normal distribution and the transformed log-estimates is

$$\log(estimate) \pm Z_{\frac{\alpha}{2}}\sqrt{V[log(estimate)]}$$

Hence the estimated survival times is given by

$$\hat{S}(t) = e^{-0.0256t^{1.156}}$$

The confidence interval based on each of the estimated Weibull parameters are more accurately constructed in logarithmic transformation

A log-transformation yields $\log(\hat{\lambda}) = -3.662$ and

$$Var\ (\log(\hat{\lambda})) = \frac{1}{\hat{\lambda}^2} Var(\hat{\lambda}) = 0.066$$

$\log(\hat{\gamma}) = 0.0145$ with estimated variance

$$Var\ (\log(\hat{\gamma})) = \frac{1}{\hat{\gamma}^2} Var(\hat{\gamma})$$

= 0.0039

An approximate 95% confidence interval based on the normal distribution and the transformed log-estimates is

$$\log(estimate) \pm Z_{\frac{\alpha}{2}}\sqrt{V[log(estimate)]}$$ with α = 5%, $\frac{\alpha}{2}$ = 1.960

The log-transformation improves the normal distribution approximation by creating more symmetric distribution for $\log(\hat{\lambda})$, the 95% confidence interval is

$$-3.662 \pm 1.960\sqrt{0.66} = (-4.167, -3.157)$$

and for $\log(\hat{\gamma})$, the 95% confidence interval is

$$0.145 \pm 1.960\sqrt{0.0039} = (\ 0.023, 0.267\ )$$

Exponentiating these estimated bounds yields approximate confidence intervals for the parameters as scale parameter:
$\hat{\lambda} = 0.0256$ and the 95% confidence interval is (0.016, 0.043)
$\hat{\gamma} = 1.156$ giving the 95% confidence interval as (1.023, 1.306)

The estimated mean survival time, based on the Weibull distribution is

$$\hat{\mu} = \hat{\lambda}^{-\left(\frac{1}{\hat{\gamma}}\right)}\Gamma(1 + \tfrac{1}{\hat{\gamma}})$$
$$= 0.0256^{-1/_{1.156}}(0.950)$$
$$= 22.597\ months$$

CONCLUSION

The average survival time for a cohort of infected individuals is 22.60 months approximately. Which means an individual who is diagnosed of HIV/AIDS will live for approximately 22.60 months before his/her death provided that no anti-retroviral drug is applied.
The confidence interval obtained using the normal distribution with $\alpha = 0.05$ reveals that the estimated parameters face with their repective confidence limits. Hence the estimates are reliable.

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