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# A Review on Accelerated Failure Time Models

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**Abstract**

Survival analysis is the analysis of statistical data in which the outcome variable of interest is time until an event occurs. In Statistical literature, it is observed that a good number of models have been developed for analyzing survival data or life time data .The most popular among them is the Cox Proportional Hazard (PH) model. Accelerated Failure Time (AFT) model, which is mainly used to study the reliability of industrial products can also be considered as a good alternative of Cox PH model in analyzing survival data. In this paper, the attempt has been made to present a review on Accelerated Failure Time models. Here the historical developments, technical developments and past research on AFT models are discussed.

**Keywords:** Survival data, regression model, AFT model, Cox PH model, event

## 1. BACKGROUND OF THE STUDY:

Survival analysis is the analysis of survival data in which the outcome variable of interest is time until some event occur. Events are generally referred as failure because the event may be death, disease, incident etc. Due to censored data, various statistical methods for failure data are developed. They are non-parametric methods (Kaplan-Meier method, log-rank test), semi-parametric method (Cox Proportional Hazard (PH) model), parametric model (Parametric PH model and Accelerated failure

Time (AFT)) model etc. Cox PH model is the most common approach for modeling survival data. Parametric AFT model provides an alternative to PH model for statistical modeling of survival data (Wei,1992).

AFT model is basically used in industrial fields and seldom used in the case of survival data. If the appropriate parametric form of AFT model is used then it offers a potential statistical approach in case of survival data which is based upon the survival curve rather than the hazard function. It is known as Accelerated failure time model because the term "failure" indicates the death, disease etc. and the term "Accelerated" indicates the responsible factor for which the rate of failure is increased. That factor is called "Acceleration factor". The AFT model is also known as the log-location scale model given by Lawless (1982). It is called log-location scale because the logarithm of time variable is considered. Details of this AFT model or log-location scale model will be discussed later. According to the literature found, Pike (1966) Proposed the AFT model in case of carcinogenesis data. He developed the basic statistical methodology and discussed likelihood estimation for the Weibull distribution. But in his paper he never mentioned it the name as Accelerated failure time model.

Again in 1972, Nelson and Hann , presented the failure time data in case of industrial life testing . They considered the number of hours to failure motorettes operating under various temperature. The name "Accelerated life test" came from this type I censoring study. The aim of their study was to determine the relationship between failure time data and temperature.

In survival analysis random censoring is considered. To modeling failure time data for random censoring in D.R. Cox (1972) introduced a model known as Cox Proportional Hazard (PH) model where the effect of covariates act multiplicatively on the hazard function. The Cox PH model is a semi-parametric model in which the baseline hazard function is completely unspecified. When the exact form of the parametric model is not known then the Cox PH model preferred than the other parametric models. But when the correct form of the parametric model is identified then the parametric models are more suitable than the semi-parametric or non-parametric models (Kleinbaum and Klein, 2002). The Acceleration failure time model is a parametric (AFT) model which was introduced by Cox (1972) . Kalbfleisch and Prentice (2002), introduced the semi- parametric class of survival model, which was the class of log-linear models for time T. In AFT model, the covariate effects act multiplicatively on survival time. Both the PH and AFT models are regression models. Though the parametric models are linear regression model but the difference between the linear regression model and the survival regression model is that in case of survival model the censored observations are considered .

The main objective of this paper is to review on the AFT models and its technical developments and past research in case of survival data .

## 2. INTRODUCTION OF THE MODEL:

**The Accelerated Failure Time model:**

The AFT model describes the relationship between the response variable and the survival time. In this model, the logarithms of the survival time is considered as a response variable and includes an error term which is assumed to follow a specific probability distribution. The assumption of AFT model is that the effect of covariates act multiplicatively (proportionally) with respect to the survival time.

The assumption of AFT model can be expressed as

$$s(t/x) = s_0(\exp(\beta' x)t) \quad for\ t \geq 0 \ldots\ldots (1)$$

Where $s(t/x)$ is the survival function at the time t and the $s_0(\exp(\beta' x)t)$ is the baseline survival function at the time t. From this equation (1), AFT model can states that the survival function of an individual with covariate x at the time t is same as the baseline survival function of the at the time $(\exp(\beta' x)t)$ , $where\ \beta' = (\beta_1, \ldots \beta_p)$ . The factor $\exp(\beta' x)$ is known as the acceleration factor. The acceleration factor is the key measure of association obtained in the AFT model. It is a ratio of survival times corresponding to any fixed value of survival time. From the acceleration factor one may able to know how a change in covariate values change in time scale from the baseline time scale. That is with the acceleration factor one can evaluate the effect of predictor variables on survival time. Suppose considering a comparison of survival functions among the persons taking cancer directed treatments and not taking any cancer directed treatments. The survival function of cancer directed treatments and not taking any cancer directed treatments are considered as $s_1(t)$ and $s_2(t)$ respectively.

The AFT assumption can be expressed as

$$s_2(t) = s_1(\exp(\beta' x)t) \quad for\ t \geq 0$$

Where $\exp(\beta' x)$ is the acceleration factor which compares the patients with cancer directed treatments and not taking cancer directed treatments.

If $\exp(\beta' x) > 1$, the effect of covariate is decelerated

And if $\exp(\beta' x) < 1$ , the effect of covariate is accelerated.

Cox(1972) introduced the Cox PH model. The Weibull model and the Exponential model can be derived from this model. But the other parametric models such as log-normal, log-logistic etc. are not derived from this PH model. The other parametric such as log-normal, log-logistic etc. models can be derived from the hazard function. (Kalbfleisch and Prentice, 2002).

The AFT model in case of hazard function can be expressed by

$$\lambda(t/x) = \exp(\beta' x)\, \lambda_0(\exp(\beta' x)\, t) \quad for\ all\ t \quad \ldots\ldots (2)$$

for example : In case of Exponential AFT model ,

The hazard function of exponential model is

$$\lambda(t) = \lambda \ , \ \ \lambda > 0$$

Here the hazard function is constant.

Now from the equation (2), the hazard function for Exponential AFT model is given by

$$\lambda(t; x) = \lambda \exp(\beta' x)$$

The conditional density function is

$$f(t; x) = \lambda \exp(\beta' x) \exp\big(-\lambda t \ exp(\beta' x)\big) \ldots . (3)$$

Let Y=logT and $y = \alpha + \varepsilon$ , and $\alpha = -log\lambda$ then

$$\begin{aligned} f(e^y) &= e^{-\alpha} \exp(\beta' x) \exp[-e^{-\alpha} e^y \exp(\beta' x)] \\ &= e^{-\alpha} \exp(\beta' x) \exp(-\mathrm{e}^{\mathrm{y}-\alpha} \exp(\beta' x)) \\ &= e^{-\alpha} \exp(\beta' x) \exp[-e^{\varepsilon} \exp(\beta' x)] \\ Y \quad &= \alpha - \beta' x + \varepsilon \ldots \ldots . (4) \end{aligned}$$

Where $\varepsilon$ has an extreme value distribution.

From this equation (3),it is seen that the covariates act multiplicatively with respect to the hazard function Cox (1972) .It is seen that from the equation (3) that the log-linear form in the equation(4) can be obtain and this model is called the AFT model .

The another representation of the relation between failure time and explanatory / response variable is the linear relationship between the logarithm of survival time and includes an error term which is assumed to follow a specific distribution such as exponential, weibull, log-normal, log-logistic etc. The general log-linear representation of AFT model for ith individual is given as

$$logT_i = \mu + \beta_1 x_1 + \cdots + \beta_p x_p + \sigma \varepsilon_i \ldots \ldots \ldots (5)$$

Where $logT_i$ represents the log-transformed survival time, $x_1, \ldots \ldots . . x_p$ are the explanatory variables with the coefficients $\beta_1, \ldots \ldots . . \beta_p$; $\varepsilon_i$ , is the residual or unexplained variation in the log- transformed survival times, that is the deviation of the values of $logT_i$ from the linear part of the model. $\varepsilon_i$ assumes a specific distribution and $\mu$ is the intercept and $\sigma$ is the scale parameters respectively. The initial step in fitting an AFT model is that for each$\varepsilon_i$, there is a corresponding distribution for $T_i$. If the $\varepsilon_i$, has an extreme value distribution then $T_i$ follows the weibull distribution. Again if $\varepsilon_i$ follows normal distribution then the $T_i$ follows log-normal distribution etc.

The survival function of $T_i$ can be expressed by the survival function of $\varepsilon_i$.

$$
\begin{aligned}
S_i(t) &= P(T \geq t) \\
&= P(\log T \geq \log t) \\
&= P(\mu + \beta_1 x_1 + \ldots.. + \beta_p x_p + \sigma\varepsilon_i \geq \log t) \\
&= P(\varepsilon_i \geq \frac{\log t - \mu - \beta_1 x_1 - \ldots\ldots - \beta_p x_p}{\sigma}) \\
&= S_{\varepsilon i}(\frac{\log t - \mu - \beta_1 x_1 - \ldots\ldots - \beta_p x_p}{\sigma}) \\
S_i(t) &= S_{\varepsilon i}(t)
\end{aligned}
$$

Again the cumulative hazard function of $T_i$ is

$$
\begin{aligned}
H_i(t) &= -\log(s_i(t)) \\
&= -log s_{\varepsilon i}(t) \\
&= H_{\varepsilon i}(t)
\end{aligned}
$$

**For example : Log-normal AFT model :**

If $\varepsilon_i$ has a standard normal distribution then $T_i$ is log-normally distributed. The density function of normal distribution is

$$f_{\varepsilon i}(\varepsilon) = \frac{1}{\sqrt{2\pi}} \exp - \left( \frac{\log t - \mu - \beta_1 x_1 - \ \ldots . \beta_p x_p}{\sigma}^2 \right) /2$$

The survival function of normal- distribution is

$$S_{\varepsilon i}(\varepsilon) = 1 - \Phi(\varepsilon)$$

The distribution function of normal distribution is

$$\Phi(\varepsilon) = \frac{\log t - \mu - \beta_1 x_1 - \cdots \beta_p x_p \ .}{\sigma}$$

The cumulative hazard function is

$$H_{\varepsilon i}(\varepsilon) = -\log\{1 - \Phi(\varepsilon)\}$$

And the hazard function is

$$h_{\varepsilon i}(\varepsilon) = \frac{f_{\varepsilon i}(\varepsilon)}{S_{\varepsilon i}(\varepsilon)}$$

In this way the log-normal AFT form can be derived.

## 3. REVIEW ON AFT MODELS :

The theory of AFT model has been a field of active research for last few decades as this model has vast applicability in the reliability theory and industrial experiments as well as survivorship data . In the following section, it is tried to have a bird's eye view on a lion's share of such developments.

Pike (1966) in his work suggest two distributional forms developed the statistical methodology and discussed the likelihood method of estimation for the Weibull distribution. Johnson and Kotz (1970) discussed about the estimation of parametric models and including exponential , weibull, log-normal, gamma, log-logistic. Lawless(1982) presented and illustrated the statistical methods for modeling and analyzing life time data. He used the term "log-location scale" model instead of Accelerated failure time model because the logarithm of the survival time was considered. Vanderhoef (1982) in his work applied a parametric method which was presented for the analysis of current status data based on AFT model and maximum likelihood estimation. In the paper it seemed that the Weibull distribution model provided a well fitting model. Cox and Oakes (1984) showed that the Weibull distribution had both proportional hazards and accelerated failure time property and Log-logistic distribution had proportional odds and accelerated failure time property.Wei (1992) introduced a non-parametric version of AFT model, which did not required the specification of a probability distribution for the survival data. Orbe et al. (2002) described that AFT model could be an interesting alternative to the Cox PH model when PH assumption did not hold. Implementation and interpretation of the results of AFT was simple . He applied AFT to two real examples and carried out a simulation study and AFT model lead to more precise results. Nardi and Scheme (2003) compared Cox PH and parametric models in three clinical trial studies mainly performed at Vienna University Medical School. They used Normal –deviate residuals (Nardi,1999) to verify the parametric model assumptions. Their study showed that Weibull model was superior to other parametric models. Pourhoseingholi et al., (2007) compared Cox regression and Parametric models in the analysis of the patients with gastric carcinoma and found that lognormal model fitted better than other models . Sayehmir et al.,(2008) studied prognostics factors of survival time after hematopoietic stem cell transplant in acute lymphoblastic leukemia patients in Shariati Hospital , Teharan and found that Weibull AFT model was superior to Cox PH model. Qi (2009) compared PH and AFT models and suggested that the Cox PH model may not be appropriate in some situations and that the AFT model could provide a more appropriate description of the data. Ravangard et al.,(2011) compared Cox PH model and the parametric models in studying the length of stay in a Tertiary Teaching Hospital in Tehran and showed that Gamma AFT model was best fitted for that data. Khanel et al., (2012) identified the important prognostic factors of Acute Liver Failure patients in India by applying AFT models and found that Log-normal

AFT was well fitted for that data in comparison to log-logistics. Vallinayagam et al., (2014) compared parametric models including Weibull and Log-normal with Cox PH model for bone- marrow transplantation data and Log-normal model was better fit than the other models. Nawumbeni et al., (2014) compared Cox PH and AFT models in HIV/TB Co-infection survival data and revealed that Gamma model was well fitted to the Co-infection data.

## 4. ESTIMATION OF ACCELERATED FAILURE TIME MODEL:

AFT models are fitted by using maximum likelihood estimation (MLE) method. The likelihood of n observed survival times $t_1, \dots \dots . . t_n$ is

$$L = \prod_{i=1}^{n} \{f_i(t_i)\}^{\delta_i} \{s_i(t_i)\}^{1-\delta_i}$$

Where $f_i(t_i)$ and $s_i(t_i)$ are the density function and the survival function for the ith individual at the time $t_i$ respectively. $\delta_i$ is the event indicator for the ith individual

$$\delta_i = \begin{cases} 1, & if\ the\ ith\ observation\ is\ event \\ 0, & if\ the\ ith\ observation\ is\ censored \end{cases}$$

Now

$$S_i(t_i) = S_{\varepsilon_i}(z_i)$$

Where,

$$z_i = \frac{logT - \mu - \beta_1 x_1 - \cdots \beta_p x_p}{\sigma}$$

The log-likelihood function is given by

$$logL = \sum_{i=1}^{n} \sigma t_i^{-\delta_i} \{f_{\varepsilon i}(z_i)\}^{\delta_i} \{s_{\varepsilon i}(z_i)\}^{1-\delta_i}$$

$$logL = \sum_{i=1}^{n} -\sigma_i \log(\sigma t_i) + \delta_i log\{f_{\varepsilon i}(z_i)\} + (1-\delta_i) log\{s_{\varepsilon i}(z_i)\}$$

Where $z_i = \frac{logt - \mu - \beta_1 x_1 - \cdots . \beta_p x_p}{\sigma}$ and MLE of (P+2) unknown parameters , $\mu, \sigma\ and$ $\beta_1, \dots \dots . . \beta_p$ are found by maximizing the log-likelihood function using Newton Raphson procedure.

**Estimation of parameters for the Weibull AFT model without covariates.**

The density function of Weibull AFT model is

$$f(y;\mu,\sigma) = \frac{1}{\sigma}\ \exp(y-\mu)\,/\sigma\ \exp(-\exp(y-\mu)/\sigma)$$

Where $-\infty < y < \infty$.

If the $\varepsilon_i$ follows the extreme value distribution then $T_i$ follows the Weibull distribution.

The survival function and the density function of the extreme value distribution are respectively

$$s(z_i) = \exp(-\exp(z_i))$$

$$\log\big(s(z_i)\big) = -\exp(z_i)$$

$$\frac{\partial \log\big(s(z_i)\big)}{\partial z_i} = -\exp(z_i)$$

$$f(z_i) = \exp(z_i)\exp(-exp(z_i))$$

$$logf(z_i) = z_i - \exp(z_i)$$

$$\frac{\partial \log\big(f(z_i)\big)}{\partial z_i} = 1 - \exp(z_i)$$

The likelihood function is

$$L = \frac{1}{\sigma}\Big[\ \prod_{i=1}^{n}\{f_i(t_i)\}^{\delta_i}\{s_i(t_i)\}^{1-\delta_i}\ \Big]$$

The log-likelihood function is

$$logL = \sum_{i=1}^{n}\delta_i \log\left(\frac{1}{\sigma}\right) + \delta_i\sum_{i=1}^{n}\log\{f_{\varepsilon i}(z_i)\} + (1-\delta_i)\sum_{i=1}^{n} log\{s_{\varepsilon i}(z_i)\}$$

$$logL = -rlog\sigma + \delta_i\sum_{i=1}^{n}\log\{f_{\varepsilon i}(z_i)\} + (1-\delta_i)\sum_{i=1}^{n} log\{s_{\varepsilon i}(z_i)\}$$

$$= -rlog\sigma + \ \delta_i\sum_{i=1}^{n}\log\{\exp(z_i)\exp(-exp(z_i))\}$$

$$+ (1-\delta_i)\sum_{i=1}^{n}\log\{\exp(-\exp(z_i))\}$$

$$= rlog\sigma + \sum_{i=1}^{n} ( \delta_i z_i - \exp(z_i)) \ldots. \quad (6)$$

Differentiating this equation (6) with respect to parameters $\mu$ and $\sigma$ one can get the parameters values of Weibull AFT model.

In this way the parameters of the AFT models can be estimated.

## 5. MODEL CHECKING:

To check the appropriate distribution of the AFT model various methods have been used. They are such as Akaike Information Criterion ( AIC), Baysian Information Criteria( BIC), etc.

(i) **AIC:** To compare various semi-parametric and parametric models Akaike Information Criterion (AIC) is used. The AIC is proposed by Akaike (Akaike, 1974). It is a measure of goodness of fit of an estimated statistical model. For the model in this study, AIC is computed as follows

$$AIC = -2(log - likelihhod) + 2(P + K)$$

Where P is the number of parameters and K is the number of coefficients (excluding constant) in the model. For P=1, for the exponential, P=2, for Weibull, Log-logistic, Lognormal etc. The model which as smallest AIC value is considered as best fitted model.

(ii) **BIC:** The Baysian Information Criteria (BIC) is given by Schwarz (Schwarz, 1978). It is computed as follows

$$BIC = -2(log - likelihood) + (P + K) * \log(n)$$

Where P is the number of parameters in the distribution, K is the number of coefficients and log(n) is the number of observations. The distribution which has the lowest BIC value is considered as best fitted model.

**(iii) Cox Snell-Residual:** the Cox – Snell Residuals can by used to check the goodness of fit of the model which was given by Cox and Snell ( Cox and Snell, 1968). The Cox- Snell residual for the ith individual with observed time t is defined as

$$\boldsymbol{r_{c_i}} = \boldsymbol{\widehat{S}_i(t)} = \boldsymbol{S_{\varepsilon_i}}\left(\frac{logt - \mu - \beta_1 x_1 - \cdots . \beta_p x_p}{\sigma}\right)$$

where the parameters are already defined above. The Cox- Snell residual can applied in any of the parametric AFT model.

## 6. CONCLUSION:

From the above discussion, it is observed that the AFT models which is widely used in analyzing industrial data can also provide a good alternative of the Cox PH model. If the correct form of the parametric model is known, then the AFT model has a vast scope for the future researchers. This model is comparatively easy to interpret. A number of research studies have already been conducted by using the AFT model which provides fruitful results.

There is a scope for further development of the AFT model. Till now, AFT model has been fitted for distributions like exponential, weibull, log-normal, log-logistic, gamma etc. One can use other distributions such as skew-normal, generalized exponential etc. to model survival data. In AFT model, the dependent variable is log of the survival time T. The dependent variable can also be used by other strictly increasing function which is also the further scope of the study.

## REFERENCES:

[1] Akaike H(1974).: A New Look at the Statistical Model Identification. *IEEE. Transaction and Automatic Control AC*-19, pp. 716-23.

[2] Cox D.R., and Snell E.J(1968).: A General Definition of Residuals (with discussion), *Journal of the Royal Statistical Society,* A. .

[3] Cox, D.R(1972). : Regression Models and Life Tables, *Journal of the Royal Statistical Society, Series B, (Methodological)*, ,Vol 34, No. 2, 187-220.

[4] Cox and Oakes(1984): Analysis of Survival Data, Chapman and Hall, London – New York.

[5] Kleinbaum,G.David and Klein, Mitchel(1996) : Survival Analysis : A Self-Learning Text , Second Edition,, Springer, New York .

[6] Khanal Prasad, Shankhar , Sreenivas,V. and Acharya,K. Subrat (2014) : Accelerated Failure Time Models: An Application in the Survival of Acute Liver Failure Patients in India, *International Journal of Science of Research (IJSR),* ISSN: 2319-7064,Impact Factor(2012):3.358,Volume 3, Issue 6,June 2014, pp 161-166.

[7] Kalbfleisch, John D. and Prentice , Ross L.(2002) : The Statistical Analysis of Failure Time Data, *John Wiley & Sons, Inc.*

[8] Lawless, J. F.(1982) : Statistical Models and Methods for Lifetime Data Analysis, *Wiley, New York.*

[9] Nelson, W.B. and Hahn, G.J.(1972) : Linear Estimation of a Regression Relationship from Censored data: 1,Simple Methods and Their Applications (With Discussion), *Technometrics,14,247-276.*

[10] Nardi, Alessandra and Schemper, Michael(2003) : Comparing Cox and Parametric models in Clinical Studies, *Statistics in Medicine, Statist Med.*; 22:3597-3610.

[11] Nawumbeni, Ngbandor Derek , Luguterah, Albert and Adampah, Timothy(2014): Performance of Cox Proportional Hazard and Accelerated Failure Time Models in the Analysis of HIV/TB Co-infection Survival Data, *Research on Humanities and Social Sciences,* ISSN (Paper)2224-5766 ISSN (Online)2225-0484 (Online), Vol.4, No.21, pp 94-102.

[12] Orbe Jesus, Ferreira Eva and Nunez- Antion, Vicente (2002): Comparing Proportional Hazards and Accelerated Failure Time models for Survival Analysis, *Statistics in Medicine.* 21: pp 3493-3510.

[13] Pike M.C.: A Method of Analysis of a Certain Class of Experiments in Carcinogenesis, Biometrics 22(1966), 142-161.

[14] Pourhoseingholi,M.A.,E. Hajizadeh,B.Moghimi Dehkordi, A. Safaee,A. Abadi and M.R. Zali (2007) : Comparing Cox regression and parametric models for survival of patients with gastric carcinoma, *Asian Pacific Journal of Cancer Prevention* ; 8 (3):412-416

[15] Qi,Jiezhi, (2009): Comparison of Proportional Hazards and Accelerated Failure Time Models, A Thesis Submitted to the College of Graduate Studies and Research in Partial Fulfillment of the Requirements for the Degree of Master of Science in the Department of Mathematics and Statistics University of Saskatchewan Saskatoon, Saskatchewan.

[16] Ravangard, R., Arab M., Rashidian, A.,Akbarisari, A., Zare A., Zeraat, H. (2011): Compared Cox Model and Parametric Models in the Study of Length of Stay in a Tertiary Teaching Hospital in Tehran, Iran. *Acta MedicaIranica*, 49(10): 650-658. Stacy(1962):

[17] Schwarz, Gideon E.(1978) : Estimating the Dimension of a Model, *The Annals of Statistics,* vol 6, No.2, 461-469.

[18] Sayehmiri, K., Eshraghian R. M., Mohammad K., Alimoghaddam K., Foroushani R. A., Zeraati H., Golestan, A., Ghavamzadeh, A. (2008): Prognostic Factors of Survival time after Hematopoietic Stem Cell Transplant in acute Lymphoblastic Leukemia Patients in Shariati Hospital, Tehran , *Journal of Experimental & Clinical Cancer Research,* **27**(1): 1-9.

[19] Vanderhoeft , Camille and Vanderhoeft , Camille (1982) : Accelerated Failure Time Models: An Application To Current Status Breast- Feeding Data From Pakistan ,Vol.38, No. 1 / 2 ( Gennaio- Giugno), pp. 135-157.

[20] Vallinayagam, V., Prathap, S., and Venkatesan, P. (2014): Parametric Regression Models in the Analysis of Breast Cancer Survival Data , *International Journal of Science and* Technology*,* 3(3) 2049-7318.

[21] Wei, L.J.: The Accelerated Failure Time Mode: A Useful Alternative To the Cox Regression Model in Survival Analysis, *Statistics in Medicine,*11, 1992, 1871-1879.