

On the Generalised Piecewise Constant Hazard Model with Application to Breast Cancer

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Abstract. In survival analysis, a baseline hazard function is combined with hazard multipliers which depend on covariate values through a logarithmic link function and a linear predictor. Hence, the form of dependence of the hazard multipliers on covariates is usually specified. This research is focused on a way of relaxing the specification of the form of dependence of the hazard on the covariates in survival analysis using the generalised piecewise constant hazard (GPCH) model where the covariates are made ordinal. The Bayesian approach to inference is used with priors based on the parametric model which allowed for main and interaction effects using R functions. A secondary data set of breast cancer consisting of 300 patients with four complete covariates which include age, gender, mode of diagnosis and location of breast cancer from the University of Ilorin teaching hospital, Ilorin, Nigeria for a period of five years was used for illustration. The choice of prior will allow a compromise which relaxes the form of dependence of the hazard function while imposing enough structure to exploit the information in the finite data set by specifying correlations in the prior distribution between log-hazards for neighbouring covariate profiles.

Keywords: Inference, Covariates profile, Piecewise constant hazard, Prior distribution, Linear predictor.

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1. Introduction

Survival analysis is a statistical technique used for analysing data for which the variable of interest is time until an event occurs. It involves the modelling of time to event data. The event data need not be death. Survival analysis can be used in many fields of study such as engineering, medicine, health, etc. (Weiss, 2017). The simplest case of survival analysis comes from how long people live

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until death. In this case, survival analysis in medicine is used to estimate patient's chances of survival after treatment of any disease (Saroj, 2020). In other cases, the event might be time till failure or manufacture (Hu and Laio, 2017) of a machine.

Survival times are often censored (Lee and Lim, 2019), (Zhang, 2016) and (Klein and Moeschberger, 2010). Censoring is one of the differences between survival analysis and the standard regression models (Consul and Okrinya, 2018). A survival model includes two features. One of which is how the covariates are related to the distribution so that individuals can be distinguished and the other is the form of the survival distribution. This study is classified under the first feature. The proportional hazard model is well known to explore the relationship between the covariates and the hazard function (Cox, 1972) in which covariates act multiplicatively on the baseline hazards (Lefebvre and Giorgi, 2021). Most parametric and non – parametric models usually assume proportional hazard where the effects of the covariates on the hazard function stays constant over time (Ma, 2021). A parametric form for the distribution may be appropriate on the theoretical grounds but the problem with this approach is that of the inconsistent estimates of the baseline hazard when the assumed parametric form is incorrect.

Many researchers have developed techniques to test and correct non – proportional hazards (Magirr, 2020). The assumption of proportionality can be relaxed by having non - proportional hazard model. The piecewise constant hazard model is used to specify the hazard by avoiding specifying the form for the baseline hazard by dividing the time into sub intervals where the baseline hazard and the linear predictor are assumed constant in each interval (Consul and Okrinya, 2018). The piecewise constant function is a common approach to modelling time varying effects since it is flexible enough to capture any shape of baseline hazard or covariate effects using both the frequentist (Olayinka and Ishaq, 2020) and more recently the Bayesian approach (Consul and Okrinya, 2018).

The proportional hazard model assumption fails to explain data related to non – linear effects of covariates (Saha-Chaudhri and Juwara, 2020). Non-linearity in models is usually handled through transformations and then estimation of linear models (Enesi and Oyejola, 2020). Procedures like the general additive models (GAMs) have been used to handle complexities in covariates in different forms which is unlikely with the usual Cox model. (Enesi and Oyejola, 2020) proposed using modified piecewise additive hazard model where he assumed three levels of variance of Weibull distribution for baseline hazards in generating data. They also incorporated the functional form of continuous covariates in a non-proportional hazard framework.

This research will further focus on exploring the relationship between the covariates and the hazard function by introducing the generalised piecewise constant hazard (GPCH) model which generalises the piecewise constant hazard model in which quantitative variables as well as time are made ordinal. The research will aim at relaxing this relationship by removing the usual assumptions of proportionality.

2. Materials and methods

2.1 Modelling in survival analysis

A standard problem in survival analysis is to make inference for covariate effects and baseline hazards from life time or survival data. The hazard function in survival analysis plays a central role. The proportional hazard model (PHM) is well known to explore the relationship between the covariates and survival (Cox, 1972). This is the most commonly used method to relate the hazard function to the explanatory variables of an individual (Consul and Okrinya, 2018). The proportional hazard model uses the assumption of proportionality in which the hazard of a particular individual is a fixed proportion of the hazard of another individual and hence, the proportional hazard model depends on the covariates and not on the time. The baseline hazard function is combined with hazard multipliers which depend on covariate values through a logarithmic link function and a linear predictor.

Suppose that we have S covariates for $s = 1, \dots, S$ and n individuals for $i = 1, \dots, n$. The covariate vector for the i^{th} individual is denoted by $\underline{X}_i$ and given as

$$\underline{X}_i = (1, x_{i,1}, x_{i,2}, \dots, x_{i,S}) \quad (1)$$

The proportional hazard model is given by

$$h_i(t) = \lambda_i \times h_0(t) \quad (2)$$

where $h_0(t)$ is the baseline hazard function which is a function of time t and does not involve the covariate $\underline{X}_i = (1, x_{i,1}, x_{i,2}, \dots, x_{i,S})$. The quantity λ_i (which is greater than 0) is the hazard multiplier which depends on the covariates of the i^{th} individual but not on the time variable t . The linear predictor η_i which is expressed as a logarithmic link function is given as

$$\log \lambda_i = \eta_i = \beta_0 + \sum_{s=1}^S \beta_s x_{i,s} \quad (3)$$

where $x_{i,s}$ is the value of covariate s for the i^{th} individual, β_0 is the baseline parameter and β_s is the covariate effect of the s^{th} covariate.

2.2 The piecewise constant hazard model (PCH)

The piecewise constant hazard (PCH) model is one of the most popular and easily used models for a semi-parametric approach to survival modelling (Breslow, 1974) and (Olayinka and Ishaq 2020). It is very useful over classical survival methods. The piecewise constant hazard (PCH) model is flexible and relaxes the assumption of a particular form for the baseline hazard by having sub-divided time where the baseline hazard and the linear predictor are assumed constant in each interval (Consul and Okrinya, 2018).

Saroj (2020) described the piecewise constant hazard model using an under-five mortality data. It is also usual that manufacturing machines work under piecewise constant operating condition which are subject to imperfect preventive maintenance. Hu and Liao (2017) developed the manufacturing machine working under piecewise constant operating condition by combining an aged-based hybrid imperfect preventive maintenance model and an accelerated failure time model.

The time t in the PCH model is partitioned into J disjoint intervals with $J - 1$ cut points given as $0 = \tau_0 < \tau_1 < \tau_2 < \dots \tau_{J-1} < \tau_J = \infty$. It became evident that the PCH model allows the baseline hazard to change at points but the coefficients of the covariates do not change. The implication therefore, is that this is still a proportional hazard model. Consul and Okrynya (2018) investigated the problem of non - proportionality in a data using the piecewise constant hazard model with time varying covariate effects where the effects of the covariates were allowed to vary over time. The hazard function for the i^{th} individual in the j^{th} interval, $h_{i,j}(t)$ for $j = 1, 2, \dots, J$ for the piecewise constant hazard model with time varying covariate effects is given by

$$h_{i,j}(t) = h_{0,j}(t) \exp \left\{ \sum_{s=1}^S \beta_{j,s} x_{i,s} \right\} \quad (4)$$

where $x_{i,s}$ denotes the value of the covariate s for the i^{th} individual and $\beta_{j,s}$ is the covariate effect for the covariate s in the j^{th} interval.

2.3 A generalisation of the piecewise constant hazard model

In this section, the relaxation of the form of the dependence of the hazard function on the covariate effects is introduced using a new model. In it, the generalised piecewise constant hazard (GPCH) model in which quantitative covariates as well as time are categorised or made ordinal.

Recall that the piecewise constant hazard model was discussed in Section 2.2 as a model that relaxes the baseline hazard. In the standard piecewise constant hazard model, the time variable is divided into intervals in which the hazard is constant. The generalised piecewise constant hazard (GPCH) model is one form of the piecewise constant hazard model in which the parametric assumption of the relationships among the covariates is relaxed. In the GPCH model, the quantitative covariates as well as the time variable are made ordinal and thus, the covariate space is divided into cells within each of which the hazard is constant. The time variable indicates the period in which the individual had the event or was censored. It is treated as another ordinal covariate except that an individual can appear in several time intervals. The time intervals therefore are incorporated just as in the case of the standard piecewise constant hazard model. The “covariate profile” is then defined as a specific list of values for the categorised covariates and a “cell” as a combination of a covariate profile and the time interval.

Suppose that we have “S” covariates in the model. Let the number of levels of

covariate s be p_s . Then, each covariate profile is associated with a unique node in a S -dimensional array in the covariate space containing $P = \prod_{s=1}^S p_s$ nodes. Combining this covariate space with the J time intervals in the PCH, will give a $S + 1$ dimensional array with $J \times P = c$ cells. A constant hazard is associated with each cell. The collection of all log-hazards is defined as

$$\underline{\eta} = (\underline{\eta}_1^T, \underline{\eta}_2^T, \dots, \underline{\eta}_P^T)^T \quad (5)$$

where $\underline{\eta}_p = (\eta_{p1}, \dots, \eta_{pJ})^T$ and η_{pj} is the log hazard for covariate profile p in the time interval j for $p = 1, \dots, P$ and $j = 1, \dots, J$. Now, the process leads to the following definition

$$\tilde{\underline{\eta}} = (\tilde{\underline{\eta}}_1^T, \dots, \tilde{\underline{\eta}}_J^T)^T \quad (6)$$

where $\tilde{\underline{\eta}}_j = (\eta_{j,1}, \dots, \eta_{j,P})^T$. such that $\tilde{\underline{\eta}}$ is in arranged form of $\underline{\eta}$ so that we have covariate profiles nested within time interval. This can be expressed as follows:

$$\underline{\eta} = H \tilde{\underline{\eta}} \quad (7)$$

where H is a permutation matrix. The Bayesian approach to inference is used. Hence, we discuss the likelihood contribution and the choice of a suitable prior distribution in the model.

2.3.1 The likelihood contribution in the generalised piecewise constant hazard model

Similar to the thought process in the case of the PCH model, the likelihood contribution in the j^{th} time interval for the k^{th} individual with profile p is related to $L_{j,p,k}$. Hence, the overall likelihood is given as

$$L = \prod_{j=1}^J \prod_{p=1}^P \prod_{k=1}^{n_p} L_{j,p,k} = \prod_{j=1}^J \prod_{p=1}^P L_{j,p} \quad (8)$$

where n_p is the number of individuals in profile p .

The individuals are labelled $i = 1, \dots, n$ the covariate profiles are labelled $p = 1, \dots, P$ the time intervals as $j = 1, \dots, J$ and the individuals in the subset with covariate profile p are labelled $k = 1, \dots, n_p$. The number of individuals with profile p who die will be denoted by $n_{d,p}$. The number of individuals with profile p who die in time interval j will be denoted by $n_{d,j,p}$.

Therefore, the individual definition is as follows:

$$\delta_{j,p,k} = \begin{cases} 1 & \text{if the } k^{th} \text{ individual in profile } p \text{ dies in interval } j \\ 0 & \text{otherwise} \end{cases}$$

Now, it becomes

$$L_{j,p} = \left\{ \prod_{k=1}^{n_p} \lambda_{j,p}^{\delta_{j,p,k}} \right\} \exp \left\{ -\lambda_{j,p} \sum_{k=1}^{n_p} t_{j,p,k}^* \right\} = \lambda_{j,p}^{n_{d,j,k}} \exp \{ -\lambda_{j,p} T_{j,p}^* \} \quad (9)$$

where $\lambda_{j,p} = \exp \{ \eta_{j,p} \}$, $T_{j,p}^* = \sum_{k=1}^{n_p} t_{j,p,k}^*$ and

$$t_{j,p,k}^* = \begin{cases} 0 & \text{if } t_{p,k} < \tau_{j-1} \\ t_{p,k} - \tau_{j-1} & \text{if } \tau_{j-1} < t_{p,k} \leq \tau_j \\ \tau_j - \tau_{j-1} & \text{if } \tau_j < t_{p,k} \end{cases}$$

The overall likelihood contribution can then be written as

$$\begin{aligned} L &= \prod_{j=1}^J \prod_{p=1}^P \lambda_{j,p}^{n_{d,j,p}} \exp \{ -\lambda_{j,p} T_{j,p}^* \} \\ &= \left\{ \prod_{j=1}^J \prod_{p=1}^P \lambda_{j,p}^{n_{d,j,p}} \right\} \left\{ \exp \left[- \sum_{j=1}^J \sum_{p=1}^P \lambda_{j,p} T_{j,p}^* \right] \right\} \end{aligned} \quad (10)$$

2.3.2 A choice of prior distribution for the generalised piecewise constant hazard model

The prior belief is such that the parameters of a model have no reference to the data and it is therefore expressed in the form of probability density function. In this model, a prior distribution in which the log - hazards in neighbouring time intervals or covariate profiles are positively correlated will be used in the generalised piecewise constant hazard model. The choice of a suitable prior distribution will be based on a parametric model.

The structure of the prior of the GPCH model will allow for main and interaction effects and we would expect that neighbouring time intervals are correlated in their prior interaction.

Suppose that $\underline{\eta}^* = (\eta_1, \dots, \eta_P)^T$ is the log-hazard in the first-time interval for the P covariate profiles and $X = x_1, \dots, x_{S'}$ be a design matrix of the data. We recall that the vector of the parameters of the linear model $\underline{\beta}$ will also have S' parameters. Then, we have that

$$\underline{\eta}^* = X \underline{\beta}. \quad (11)$$

If the expectation of $\underline{\beta}$ is $(\underline{\beta})$ then the expectation of $\underline{\eta}^*$ is

$$\underline{\mu}^* = X(\underline{\beta}) \quad (12)$$

Let the covariance matrix of $\underline{\beta}$ be $V_{\underline{\beta}}$. Then, the covariance matrix of η^* is

$$(\underline{\eta}^*) = X V_{\underline{\beta}} X^T \quad (13)$$

There is also the need to consider the dependence between parameters in different time intervals. One possible way of constructing the joint prior distribution of the c parameters of the model might be to give it either a stationary first order autoregressive process prior or a moving average process prior. The assumption here will be a first order autoregressive model AR(1) (Chatfield, 2004) and so, we choose an autoregressive parameter ρ which gives different strength of relationship to the parameters. If the autoregressive parameter is positive then the collection of parameters that are closer to each other are more strongly correlated. Hence, the autoregressive parameter governs the degree of prior correlation between neighbouring time periods. The auto-covariance at lag j for $j = 1, \dots, J$ is given by $\rho^j(\underline{\eta}^*)$.

Hence, a covariance matrix of the log-hazards as shown below will be given with covariate profiles nested within the time intervals.

$$(\underline{\eta}^*) = \begin{bmatrix} V_0 & V_1 & V_2 & V_3 & \cdots & V_{J-1} \\ V_1 & V_0 & V_1 & V_2 & \cdots & V_{J-2} \\ V_2 & V_1 & V_0 & V_1 & \cdots & V_{J-3} \\ V_3 & V_2 & V_1 & V_0 & \cdots & V_{J-4} \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ V_{J-1} & V_{J-2} & V_{J-3} & V_{J-4} & \cdots & V_0 \end{bmatrix}$$

where V_0 is $(\underline{\eta}^*) + (\gamma)$ and (γ) is a $J \times J$ diagonal matrix which is the covariance matrix of the interactions effects of the covariate profiles and V_k is $\rho^k(\underline{\eta}^*)$ for $k > 0$.

Consequently, $(\underline{\eta}^*)$ is rearranged to have a covariance matrix for the vector of η in which the time intervals are nested within the covariate profiles. Hence, the re-ordered matrix as shown in (14).

$$(\underline{\eta}^*) = H(\underline{\eta}^*)H^T \quad (14)$$

Again, H is a permutation matrix, which means the means of the parameters are now made not to depend on the time interval so that they are the same at every time interval and then the prior is stationary. Again, the means of the parameters can be rearranged so that the time intervals are within the covariate profiles. Therefore $\underline{\mu}$ is got from $\underline{\mu}^*$. The joint prior distribution of the parameters of the model now has a prior mean of $\underline{\mu}$ and covariance matrix $(\underline{\eta})$.

2.4 Sampling of the logarithm of the hazards

The Bayesian approach to inference will be used for sampling the logarithm of the hazards (log-hazards). Bayesian inference requires the combination of prior experience (which is in the form of prior probability) and the observed data

(which is in the form of a likelihood). Therefore, the posterior distribution combines the likelihood and the prior which captures all that is known about the parameters. The Bayesian inference often involves calculations which are analytically intractable. In this context, the Markov Chain Monte Carlo (MCMC) algorithm (Ibrahim and Sinha, 2001), which involves sampling the log-hazards one at a time is applied. The MCMC algorithms include Metropolis and Metropolis Hasting algorithm, Gibbs Sampler and Metropolis within Gibbs algorithm. The Metropolis within Gibbs sampler is used.

This method goes through each unknown and samples directly from the corresponding full conditional distribution where sampling is done from a suitable proposal distribution and either accept or reject the proposal value according to a Metropolis Hasting acceptance rule. To this end, the conditional prior distribution of each log-hazard will be used given the others using the basic properties of the normal distribution (Rue and Held, 2005).

The conditional prior density for the p^{th} log-hazard representing a covariate profile at a time interval, η_p is then given by

$$\pi(\eta_p) \propto \exp \left\{ -\frac{1}{2} \frac{(\eta_p - \mu_{p|p'})^2}{V_{p|p'}} \right\}$$

where $\mu_{p|p'}$ and $V_{p|p'}$ are the conditional mean and variance of the log-hazard. The full conditional distribution of the p^{th} log-hazard η_p is

$$\begin{aligned} \pi(\eta_p|D) &\propto \text{prior} \times \text{likelihood} \\ &= (\text{constant})\pi(\eta_p)L_{j,p} \end{aligned}$$

where D is the data.

A new value of η_p , η_p^* is proposed from a normal distribution and the proposal density of η_p^* given η_p , $q(\eta_p^*|\eta_p)$ and the proposal density of η_p given η_p^* , $q(\eta_p|\eta_p^*)$. From the Metropolis-Hastings algorithm, the proposed log-hazard η_p^* is accepted with probability

$$A = \min \left\{ 1, \frac{\pi(\eta_p^*|D) q(\eta_p|\eta_p^*)}{\pi(\eta_p|D) q(\eta_p^*|\eta_p)} \right\}.$$

The choice of a suitable prior distribution will be based on a parametric model. This will allow a compromise, which relaxes the form of dependence of the hazard function while imposing enough structure to exploit the information in the finite data sets by specifying correlations in the prior distribution between log-hazards for neighbouring covariate profiles. The choice of prior distribution can therefore be important for obtaining useful posterior inferences.

3. Application

The generalised piecewise constant hazard model will be applied to a data set of 300 breast cancer patients with 5 completely observed covariates which include

age, gender, mode of diagnosis and location of breast cancer from the University of Ilorin teaching hospital, Ilorin, Nigeria for a period of five years (Oguntunde and Okagbue, 2017). This database holds records of the length of stay and the status (dead or alive) after treatment from year 2011 to 2016.

3.1 An overview of explanatory variables of the Breast cancer data

The data set includes five covariates which are the age, sex, mode (mode of diagnosis), location (location of breast cancer) and time. The data consist of 97 patients who died and 203 patients who were censored. The data set includes time in days of length of stay (LOS) of the patients after treatment, which were right censored. The censoring indicator was “1” for death and “0” for censoring. The explanatory variables used in this breast data set are discussed as follows:

Age: This is the age (in years) of the patient.

Sex: This is the sex of the patient. Female was indicated as “1” while male as “2”. There were 25 males and 275 females in the data.

Mode of diagnosis (mode): This is the mode of diagnosis of the cancer. Cytological was indicated as “1” while histological was indicated as “2”.

Location of breast cancer (location): This indicates the location of the breast cancer on the survivability of the breast cancer patients. Left breast was indicated as “1”, right breast was indicated as “2” and both breast was indicated as “3”.

Time: This is the time in days of length of stay of the patients after treatment.

3.2 Application to dataset using priors based on parametric model

The generalised piecewise constant hazard model is now applied to the breast cancer data set. The time variable is measured in units of days. The ordering of the covariates is given in Table 1.

Table 1: Ordering of covariates for the breast cancer data set for GPCH model

Covariates	Notation
Age	x_1
Sex	x_2
mode	x_3
location	x_4
Time variable	x_5

The covariate Age was categorised into four groups (with cut points being the lower quartile, median and upper quartile of the covariates), Sex and mode are binary variables, location has three groups and the time variable will be divided into ten groups. The number of covariate profiles will be $4 \times 2 \times 2 \times 3 = 48$.

The linear predictor for the p^{th} covariate profile in the j^{th} time interval is defined as

$$\eta_{p,j} = \beta_{0,j} + \beta_{a',j}, x_{p,1} + \beta_{s',j}, x_{p,2} + \beta_{m',j}, x_{p,3} + \beta_{l',j}, x_{p,4} + \gamma_{x_{p,1}, x_{p,2}, x_{p,3}, x_{p,4}, j}$$

where $\beta_{a',j}$, $\beta_{s',j}$, $\beta_{m',j}$ and $\beta_{l',j}$ depend on the categorical value of “age”, “sex”, “mode” and “location” respectively. Thus, the vector of covariate coefficients of the parametric model is $= (\beta_0, \beta_{a'}, \beta_{s'}, \beta_{m'}, \beta_{l'})^T$.

There will be 8 parameters in the linear model, including an intercept. In the construction of the prior of the covariate effects, we avoid over parameterisation since all covariates are categorical. For instance, we have that $\delta_{a',1}$, $\delta_{a',2}$ and $\delta_{a',3}$ for the coefficient of age. Following Farrow (2011), the prior distribution of the parameters is constructed as given in Table 2.

Table 2: The prior means and variances for the parameters of the Breast cancer data set

Parameter	prior mean	prior variances
β_0 (baseline parameter)	-6	0.12
$\delta_{a',1}$	0.000	0.02
$\delta_{a',2}$	0.000	0.06
$\delta_{a',3}$	0.000	0.003
$\delta_{s'}$	0.000	0.0625
$\delta_{m'}$	0.000	0.06
$\delta_{l',1}$	0.000	0.02
$\delta_{l',2}$	0.000	0.001

Accordingly, the prior vector of prior means $\underline{\mu}^*$ and covariance matrix $(\underline{\eta}^*)$ of the log hazards are equally constructed. The contribution of the right censored observation to the likelihood is usually the survival function. In the case of the generalised piecewise constant hazard model, the assumption is that associated with every patient is a time which could either be a death or censoring time. Every interval is associated with three different groups of patients; patients who died during the interval, patients who were censored during the interval and patients who survived during the interval. The contribution of the likelihood from the patients in every interval will depend on the three different groups of patients. Recall that the likelihood contribution in the j^{th} time interval for the k^{th} individual with profile p is written as $L_{j,p,k}$. Hence, the overall likelihood is as given in (10).

4. Results and discussions

The Metropolis within Gibbs algorithm can be applied here. The R functions (R Development Core Team, 2008) was used for the computation. Following a burn-in of 50000 iterations, 100000 iterations were taken. The posterior means and variances of some of the log-hazards are given in Table 3. The posterior means and variances of some of the log - hazards for the parameters of the breast cancer data set.

In the generalised piecewise constant hazard model, the choice of prior allowed a compromise that relaxed the form of dependence of the hazard function on the covariates while imposing enough structure to exploit the information in the data set by specifying correlations in the prior distribution between log-hazards

Table 3: The posterior means and variances of some of the log - hazards for the parameters of the breast cancer data set

Parameters	Posterior mean	Posterior variance
η_1	-2.173	0.00019
η_2	-2.097	0.00056
η_3	-2.023	0.00045
η_4	-2.013	0.00038
η_5	-2.027	0.00018
η_6	-2.082	0.00025
η_7	-1.950	0.00019
η_8	-1.967	0.00007
η_9	-1.930	0.0019
η_{10}	-2.008	0.0005

for neighbouring covariate profiles.

It is important to discuss the strength and weakness of the GPCH model compared to other models like the usual proportional hazard model. One major advantage of the GPCH model over most methods used in Bayesian inference is the possibility of forming and combining the marginal variances of the covariate profiles to reflect a reasonable assessment of our prior uncertainties. In the GPCH model, the corresponding hazard is constant within cells. The model has the flexibility of deciding on the choice of the number of cut points and hence, avoid having too many parameters in the model. Another advantage of the GPCH model is the flexibility to exploit the Markov property within cells by using the Gibbs sampling where a particular log-hazard corresponding to a cell can simply be sampled by conditioning on the neighbours.

One weakness of the GPCH model is the problem of the choice of the number of categories of the ordinal covariates. However, in this work each continuous covariate have been partitioned into four groups and the lower quartile, median and upper quartile were used as the cut points of the covariates. The range of the observations of the covariate of interest could as well be partitioned into four intervals of equal width and then use these groups as the categories of the ordinal covariates. Another weakness of the GPCH model is that it can be illustrated using only a data set with smaller number of covariates.

In order to determine the performance of the GPCH model, the GPCH model is compared with the proportional hazard model (PHM) based on Akaike information Criterion (AIC) value using R statistical software. The Akaike information Criterion (AIC) is a measure that is used to select a model from a set of models. The AIC is given as

$$AIC = -2 \times \log\text{likelihood} + 2 \times k \quad (15)$$

where k is the number of parameters in the model. Smaller AIC value indicates a better model fit.

The Akaike Information Criterion was calculated for both the GPCH and proportional hazard model and the values were given as 931.8117 and 974.4885

respectively. The GPCH has a smaller value in AIC while the PHM has bigger value. This proves that the GPCH model is a better fit for the breast cancer patient's data.

5. Conclusion

This research has discussed a way of relaxing the specification of the form of dependence of the hazard on the covariates in survival analysis. A Bayesian approach to the generalised piecewise constant hazard (GPCH) model using suitable priors and MCMC simulation is presented. In the generalised piecewise constant hazard model, the covariates were made ordinal and a finite number of possible covariate profiles were developed. A "cell" will be produced when the covariate profile and the time interval are combined. Then a prior distribution for the log-hazards of the covariate profiles which was based on the parametric model and allowed for main and interaction effects were used.

In the generalised piecewise constant hazard model, the number of covariate profiles will depend on the number of covariates and categories. In general, if there are many covariates with many categories, the number of covariate profiles will be huge and hence, involves fitting a model with so many parameters. There will be fewer individuals in the data set with more number of distinct covariate profiles among observed individuals. Some of the cells might not have individuals in the neighbouring cells because the cells might have no data. The GPCH model is very practicable in the case of the breast cancer data where there were only four covariates, 48 covariate profiles and 10 time periods and hence, a total of 480 cells in the range of 300 patients. The log-hazard for a cell in the multidimensional array depends on those in the neighbouring cells and hence the Markov property was be used.

The Bayesian approach to modelling accounts for right – censored survival data and the covariate effects also show posterior consistency. This approach to modelling is an important measure not only to clinicians (in determining prognosis and treatment) but also for patients and their families for decision making. The Bayesian approach will also help in the understanding of quantities that will help inform researchers render treatment to patients and assess the patient's survival.

The approach of modelling used in this research has the possibility of forming and combining the marginal variances of the covariate profiles which reflect a reasonable assessment of the prior uncertainties. In the GPCH model, we have categorised the covariates and the covariate profiles are combined with the time interval to form cells within which the corresponding hazard is constant. In this research, we have also considered the dependence between parameters in the different time intervals by supposing a first order autoregressive model and choosing an autoregressive parameter which gives the strength of relationships to the log-hazards and hence, exploiting the Markov property.

The GPCH model is particularly useful in the context in which the baseline hazard is of primary interest. The study demonstrated that the generalised piecewise hazard model offered the flexibility of the modelling of the covariate effects with ease. The model relaxed the relationship among the covariates by removing the usual assumption of proportionality. The GPCH model generalised the

piecewise constant hazard model by dividing the patients into covariate profiles with which the hazard was constant. This study also demonstrated how the choice of prior allowed for a compromise which relaxed the form of dependence of the hazard function on the covariates while it imposed enough structure to exploit the information in the data set by specifying correlations in the prior distribution between log-hazards for neighbouring covariate profiles.

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