Available online www.jsaer.com

***Journal of Scientific and Engineering Research*, 2018, 5(6):32-51**

Research Article

ISSN: 2394-2630
CODEN(USA): JSERBR

A Bayesian approach to relaxing the proportional hazard model and the form of baseline hazard in Survival Analysis with a practical application to breast cancer data

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Abstract This research is concerned with the Bayesian methodology of relaxing the proportional hazard model by having non-proportional hazard model such as a piecewise constant hazard model. The form of the baseline hazard was also relaxed using the piecewise constant hazard model. It will allow the form of the baseline hazard to change. In addition, the coefficients of the covariates can change over time and this allows for non-proportionality of hazards whereby the proportional hazard assumption will be inappropriate. We use the Bayesian approach to inference in incorporating covariates into the model using a breast cancer data.

Keywords Survival, proportional hazards, non-proportionality, prognosis indices, baseline hazard, covariate effects

1. Introduction

This research is concerned with a method of introducing flexibility to Bayesian modelling of survival analysis by relaxing the proportional hazard model and the form of the baseline hazard. The main purpose of survival analysis in medicine is to estimate a patient`s chances of survival as a function of time given the available covariates at the time the patient was admitted to the study. Thus, a standard problem in survival analysis is to explore the relationship between the covariates and survival [7] and to make inference for covariate effects and baseline hazards from life time or survival data. It is very common that to assume the proportional hazard model in which the hazard of any individual is a fixed proportion of the hazard of any other individual. This implies that the hazard ratio is dependent only on the covariates and not on the time. However, the proportional hazard model may not be suitable if the effects of the covariates take a different form and hence the form of dependence of the hazard function on the covariates should not be specified.

Most analysts start out by fitting a parametric proportional hazard model to describe the features of the data since parametric models for survival data have the advantage of being simple to handle because the visualization of the hazard function is much easier [5]. We will note that the form of the baseline hazard in these parametric models might not be simple. One limitation of assuming a proportional hazard model which is a key to its analytical simplicity in estimating the parameters is that the parameters stay constant over time thereby forcing the effects of the covariates to have the same effect at all points in time. The popular Cox semi-parametric model [7] is semi-parametric in the sense that there is a parametric model for the dependence of the hazard multipliers on the covariates but no parametric form is specified for the baseline hazard. [23] and [8] discussed modelling non-proportionality of hazards using the piecewise constant hazard model with priors for the coefficients in the linear predictor taking the form of the system evolution in a dynamic linear model. [20] extended the proportional hazard model by allowing for the non-proportionality of hazards and incorporating time varying regression coefficients. [24] used a mixture model approach to non-proportionality of hazards.

It is typical that covariates contribute linearly to the logarithm of the hazard multiplier but this may not be appropriate as a pure linear predictor may not be sufficient to capture complex relationship between covariates and survival. It may be that some non-linear function of the covariates might be more appropriate. Some possibilities for the different forms of dependence on covariates are splines [19], basis function regression, Bayesian classification and regression trees (C&RT) etc. [8]. [25] checked the assumption of linear covariate effects on survival using restricted cubic splines and Martingale residuals. [18] demonstrated how a neural network can be used to allow for non-linear predictors and covariate effects varying over time. [1] considered the application of neural networks to model non-proportionality in survival analysis.

The aim in this research is to relax the assumption of proportional hazard model by having a non-proportional hazard model and the form of baseline hazard. We discuss one way where both assumptions are relaxed using the piecewise constant hazard model. The form of the baseline hazard can also be relaxed using the piecewise constant hazard model. There is the need to relax these assumptions by removing the assumptions of parametric forms which are usually made and allowing the model to adapt to the true form of the relationship. We adopt the Bayesian approach to inference.

The rest of the paper is briefly reviews the 'usual proportional hazard model and the piecewise constant hazard model and time varying covariate effects model will be discussed as semi-parametric models. We will apply Bayesian inference to survival using piecewise constant hazard model and we will also discuss how we choose cut points, construct the likelihood and prior distribution in the piecewise constant hazard model. We discuss using the survival probability at a particular time or predictive median survival time as the prognostic index in the piecewise constant hazard model and illustrate a practical application to relaxing the proportional hazard model and the form of baseline hazard in survival analysis using breast cancer data. We give some discussions and summaries of results and conclude the research.

2. The Usual Proportional Hazard Model

The proportional hazard model is the most commonly used method to relate the hazard function to the covariate values for an individual using the proportionality assumption [7]. We suppose that we have S covariates for $s = 1, \ldots, S$ and n individuals for $i = 1, \ldots, n$. We denote the covariate vector for the i^{th} individual by $\underline{X_i} = (1, x_{i,1}, x_{i,2}, \ldots\ldots, x_{i,S})$. We will note that these covariates may be continuous, discrete, categorical or even indicator variables (equal to 1 if present and 0 if absent). The proportional hazard model assumes that any two individuals i and j with the hazard function $h_i(t)$ and $h_j(t)$ at time t and covariate vectors $\underline{X_i} = (1, x_{i,1}, x_{i,2}, \ldots\ldots, x_{i,S})$ and $\underline{X_j} = (1, x_{j,1}, x_{j,2}, \ldots\ldots, x_{j,S})$, have their hazards which is related by

$$h_i(t) = \lambda_{ij} \times h_j(t) \quad (1)$$

We have that λ_{ij} is a constant and does not depend on t. Another way of writing Equation 1 is

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

where $h_0(t)$ is the baseline hazard function which is a function of time t but does not involve the covariates $\underline{X_i} = (1, x_{i,1}, x_{i,2}, \ldots\ldots, x_{i,S})$. We have that the quantity λ_i is the hazard multiplier which depends on the covariates of the individual i but not on the time variable t. We have that $\lambda_i > 0$ and this is usually done using a logarithmic link function to a linear predictor η_i . So,

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

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

3. Piecewise Constant Hazard Model With Time Varying Covariate Effects

In this research, we will discuss the piecewise constant hazard model and time varying covariate effects model as semi-parametric models. The piecewise constant hazard model is one of the most convenient and popular models for a semi-parametric approach to survival modelling [3]. It is flexible and relaxes the assumption of a particular form for the baseline hazard by having sub-divided time where the baseline hazard $h_0(t)$ and the linear predictor are assumed constant in each interval.

In the PCH model, the time t is partitioned into J disjoint intervals with J-1 cut points given as $0 = \tau_0 < \tau_1 < \ldots.. < \tau_{J-1} < \tau_j = \infty$. The j^{th} interval is defined as $[\tau_{j-1}, \tau_j)$ for $j = 1, \ldots \ldots J$ with $\tau_0 = 0$ and $\tau_j = \infty$. The hazard is constant within each interval but is allowed to vary from one interval to another.

The proportional hazard model assumption might not be true as the effects of covariates might vary over time and it is unable to describe time varying covariate effects. The results for our model could be incorrect and hence, we have wrong conclusions if we ignore the time varying covariate effects and assume constant effects. For instance, in the piecewise constant hazard models, we allow the baseline hazard to change at points but the coefficients of the covariates do not change and in this case, it is still a proportional hazard model. However, non-proportional hazards could arise if the covariate effects change over time.

It is possible that we allow the effects of the covariates to vary over time. The piecewise constant hazard model with time varying covariates effects can be used to investigate the problem of non-proportionality present in the data. [9] allowed dependence on the covariates to change at points which make the hazards non-proportional and allow time varying covariate effects.

Suppose that we have a piecewise constant hazard model with time varying covariate effects and the hazard function for the i^{th} individual in the j^{th} interval, $h_{i,j}(t)$ for $j = 1,2, \ldots \ldots, J$ is given by

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

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

4. Bayesian Survival Modelling Using the Piecewise Constant Hazard Model

The proportional hazard model is a well-known way to conduct survival analysis because of its straight forwardness. It is possible to extend our model beyond the usual proportional hazard model since a higher degree of complexity may describe the survival analysis better. We will fit a piecewise constant hazard model which relaxes the assumption of a particular form for the baseline hazard by having sub-divided time. Here, there is flexibility in modelling of the baseline hazard and we check for time dependent covariate effects which are a form of non-proportionality of hazards.

We may wish to apply Bayesian inference to our discussions on the piecewise constant hazard model with time varying covariate effects. Much work has been done on piecewise constant hazard models where the hazard parameters are independent between intervals. See, for example [9] and [11]. In Bayesian survival analysis, our beliefs about the unknown parameters of the survival model are expressed in terms of a probability distribution in the form of the prior which is updated to the posterior distribution after seeing the data in the form of the likelihood function. In cases where the posterior distribution does not have a standard form, it is usual to sample from the posterior distribution using Markov chain Monte Carlo (MCMC) methods.

The piecewise constant hazard model requires the discretisation of the time axis into intervals and thereby choosing the number and locations of the cut points. Some authors have suggested defining the intervals as beginning and ending at the observed failure times while [13] suggested selecting intervals independently of the data. In an attempt to define intervals, [22] suggested shorter intervals over the first few years since deaths in cancer data are common in early stages and longer intervals in the later years since there are fewer deaths.

In this research, we suggest one possibility of deliberately choosing our cut points so that we expect to have the same number of deaths in each interval. We would think of a certain number of cut points and expect equal portions of death to be in each time interval using prior judgements. We will suppose that we want to choose ten time intervals and we might then think ordinarily that we should have approximately 10% of the deaths in each interval. We might also suppose that the event times will have approximately an exponential distribution. We recall that the survival function of an exponential distribution with parameter λ is given by $exp\{-\lambda t\}$. Given the cut points $\tau_1 < \ldots.. < \tau_{J-1}$, the probability of surviving until τ_j will be

$$exp\{-\lambda\tau_j\} = 1 - 0.1j$$

and $\tau_j = -\frac{1}{\lambda} log(1 - 0.1j)$

We let the mean of the distribution $\left(\frac{1}{\lambda}\right)$ be υ and $\varsigma = \frac{1}{J}$. So,

$$\tau_j = -\upsilon \, log(1 - j\varsigma)$$

We will want to construct the likelihood of a piecewise constant hazard model by supposing that associated with every patient is a time which could either be a death or censoring time and that 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 the interval. The likelihood contribution L of the patients is given as

$$L = \prod_{i=1}^{n}\prod_{j=1}^{J} L_{i,j}$$

where

$$L_{i,j} = \begin{cases} 1 & \text{if } t_i < \tau_{j-1} \\ \lambda_{i,j}{}^{\partial_{i,j}} exp\{-\lambda(t_i - \tau_{j-1})\} & \text{if } \tau_{j-1} \le t_i < \tau_j \\ exp\{-\lambda(t_i - \tau_{j-1})\} & \text{if } t_i \ge \tau_{j-1} \end{cases}$$

J is the number of time intervals

t_i is the event or censoring time of the i^{th} individual.

$\lambda_{i,j}$ is the hazard of the i^{th} individual in the j^{th} interval.

$\partial_{i,j}$ is the indicator of death or censoring of the i^{th} individual in the j^{th} interval.

We will note that within each interval the conditional survival distribution given that the patient is alive and uncensored at time τ_{j-1} is exponential since the hazard is constant.

We construct the prior distribution for the baseline parameter, β_0 and the regression parameters β_s. In a Bayesian context, we have the advantage of constructing a prior that makes the hazard parameters in neighbouring intervals to be correlated. In this research, we would use a piecewise constant hazard model which has prior distribution in which the parameters are correlated over time. [11] and [9] made the prior distribution of the parameters independent between time intervals. However, it would be reasonable to think that the hazards in the intervals which are closely together are likely to be similar.

In our illustration in this research we will assume that the prior will take the form of a realisation of a stochastic process which could either be stationary or non-stationary. We will make the priors stationary so that each parameter gets the same variance in each time period. For example, we might use an autoregressive process with autoregressive parameter which governs how strong the correlation between time periods will be. We will choose to give the autoregressive parameter $\rho > 0$ a positive autocorrelation. That is, we give a first order autoregressive process such that for any given value of autoregressive parameter, the process is given by

$$\beta_s - \mu = \rho(\beta_{s-1} - \mu) + \epsilon_s$$

where ϵ_s is normally distributed with mean zero and variance σ^2

The variance of the process is

$$Var(\beta_s) = \sigma^2 \sum_{p=0}^{\infty} \rho^{2p} = \frac{\sigma^2}{1 - \rho^2}$$

5. A Prognostic Index based on the Piecewise Constant Hazard Model

The prognostic index in a standard proportional hazard model is the linear predictor or some function of it, which is the logarithm of the hazard multiplier. A prognostic index in the case of the piecewise constant hazard model cannot be constructed in the same way as the linear predictor changes from one time interval to another. It is not obvious what the prognostic index should be in the piecewise constant hazard model. In this research, we use the survival probability at a particular time or the predictive median survival time as the prognostic index, for example.

We will need to compute the predictive survival probability in order to work out the predictive median survival time.

5.1. Computation of Survival Probability at a Fixed Time

We will use the following steps to find the predictive survival probability at any fixed time t^*. We calculate the survival probability at each cut point τ_j where $\tau_j < t^*$ for each vector of sampled parameter values. We will suppose that we have cut points $\tau_0 = 0, \tau_1 = \cdots, \tau_J \to \infty$ with J intervals and hazards $h_{i1,} h_{i2}, \dots \dots, h_{iJ}$ for a new case. We would want a predictive survival probability for a new case or a particular covariate profile. Then, the probability that the individual survives the first interval is

$$Pr(T > \tau_1) = exp\{-\tau_1 h_{i1}\}$$

Similarly, the probability that the individual survives the j^{th} interval is

$$Pr(T > \tau_j) = exp\left\{-\sum_{m=1}^{j} h_{im}(\tau_m - \tau_{m-1})\right\}$$

The stored survival probabilities are then averaged over all sampled parameters sets. The averaged survival probability is the predictive survival probability of the patient at time t^*.

5.2. Practical Computation of Predictive Median Survival Time

We will first of all find the predictive survival probability, $Pr(T > \tau_j)$ for $\tau_1, \tau_2 \dots\dots$ until $S(\tau_j) < 0.5$. An iterative method can be used to find the predictive median survival time (t_m) such that $Pr(T > t_m) = 0.5$ since we know the interval in which t_m falls. We could, for example, find where in the interval the predictive median survival time t_m is by using interval halving. We do interval halving by moving half way between the lower and the higher time limits of the interval until it eventually converges. In cases, where the predictive median survival time falls in the last interval, the upper limit would be infinity and the interval halving will not be direct. We could transform the life times to a function x where$x \in [0,1)$. However, we propose a more efficient algorithm as follows.

5.3. An Iterative Algorithm for finding the Predictive Median Survival Time

We avoid the problem of looking for the upper or lower limit and using interval halving by using the following algorithm.

Let $S(t) = Pr(T > t)$ be the predictive survival probability at time t (i.e the function evaluated at time t). Suppose that we have evaluated $S(\tau_{j-1})$ and $S(\tau_j)$ and $S(\tau_{j-1}) > 0.5 > S(\tau_j)$ so $\tau_{j-1} < t_m < \tau_j$ where t_m is the predictive median survival time.

Let $S(t|\lambda) = Pr(T > t|\lambda)$ be the survival function for a given value of λ. Now,

$S(t|\lambda) = S(\tau_{j-1})\, exp\{-\lambda(t - \tau_{j-1})\}$ for $\tau_{j-1} \le t < \tau_j$

So,

$$\log\{S(t|\lambda)\} = \log\{S(\tau_{j-1})\} - \lambda(t - \tau_{j-1})$$

which is linear in t. We use a locally linear approximation to $g(t) = log\{S(t)\}$ within$\tau_{j-1} \le t < \tau_j$. We require t_m such that $g(t_m) = \log 0.5 = -\log 2$.

Algorithm

Let $t_1 = \tau_{j-1}$. Calculate g_1 =g(t_1).

Let $t_2 = \tau_j$, if $j < J$ or $t_2 = 2\tau_{J-1}$ if $j = J$.

Calculate $g_2 = g(t_2)$.

For $k = 3,4, \dots\dots k_{max}$

{If $(t_{k-1} - t_{k-2})^2 > \partial$ then {calculate

$$b = \frac{g_{k-1} - g_{k-2}}{t_{k-1} - t_{k-2}}$$

Calculate

$$t_k = t_{k-2} - \frac{1}{b}(g_{k-2} + \log 2)$$

}

Else stop

}

6. A Practical application to Breast Cancer data

In this research, we will apply the Bayesian survival modelling using the piecewise constant hazard model to the data set provided by Saudi Cancer Registry (SCR) in King Faisal Specialist Hospital and Research Centre (KFSH & RC). The information included in the data set are survival time, censoring indicator, gender, age, marital status, address code, laterality, grade, stage (extent) and topography. The data set contains information on 5432 patients diagnosed of advanced breast cancer with eight covariates collected for 9-years (2004 to 2013). The age of the patient at diagnosis was recorded as a continuous variable. The gender of the patients was recorded with value 1 for male and 2 for female. The grade of a tumor describes how quickly a tumor can grow and spread. In our data set, the value 1, 2, 3 and 4 were used for Grade I (low grade), II (intermediate grade), III (Poorly differentiated or high grade) and IV (Undifferentiated or high grade) respectively. The extent is the stage of the disease. The values 1, 2, 3 and 4 were used to represent in situ, localised, regional and distant metastasis respectively. The laterality identities the side of a paired organ or the side of the body on which the reportable tumor originated. The values 1, 2, 3 and 4 were used to represent right, left, paired site and bilateral involve sides respectively. The address code of the patients were recorded with values 1 to 14 representing Eastern, Riyadh, Asir, Tabuk, Qassim, Madinah, Makkah, Hail, Jouf, Baha, Northern, Jazan, International and Najran respectively. The topography indicates the site of origin of a neoplasm with values 1 to 9 representing Nipple, Central portion of breast, Upper-inner quadrant of breast, Lower-inner quadrant of breast, Upper-outer quadrant of breast, Lower-outer quadrant of breast, Axillary tail of breast, Overl. lesion of breast and Breast, NOS respectively. The marital status of the patient were recorded with the values 1 to 4 used to represent married, single, widowed and divorced respectively.

We follow our discussion on the construction of the likelihood contribution and the construction of the prior. We will apply Equation (4) to the breast cancer data set to choose the cut points. We may make a prior assessment of the mean survival life time of a patient, as 5 years in the breast cancer data set, and we get the cut points as 0.527, 1.116, 1.783, 2.554, 3.466, 4.581, 6.020, 8.047, and 11.513.

We follow our discussion to construct the prior means and variances of the parameters of the breast cancer data set. We would want to think of the value of the autoregressive parameter by considering how much the variance of the parameter will reduce in the next time periods if we know the value in the first time period. We suppose that 90% of the variance in the next time period is explained. This corresponds to a coefficient of determination $r^2 = 0.9$ correlation $r = 0.95$.

Posterior distributions for the covariate effects were evaluated using the RJAGS software. Following a burn-in of 5000 iterations of the sampler, 50000 iterations were taken. Convergence was checked using two chains starting from very different values. Visual inspection of the trace plots of the covariate parameters showed that the mixing appeared very satisfactory. The posterior means and standard deviations of the parameters for each of the ten intervals are given in the Appendix. The posterior means and standard deviations for the effects of age and gender and baseline parameter β_0 for each interval are given in Table 1.

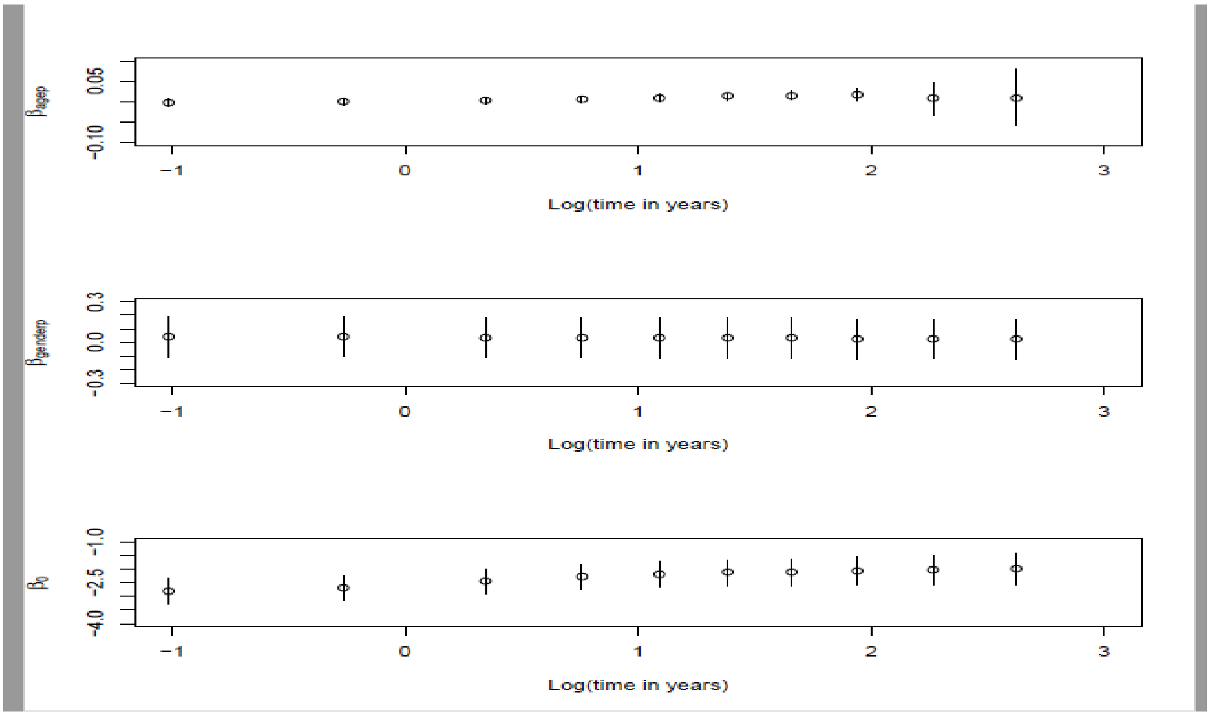
Table 1: Posterior numerical summaries of some selected parameters in each interval

j	τ_j	β_{age}	β_{gender}	β_0
1	0.527	-0.001(0.005)	0.040(0.074)	-2.800(0.238)
2	1.116	0.001(0.004)	0.040(0.072)	-2.692(0.229)
3	1.783	0.002(0.004)	0.034(0.073)	-2.444(0.224)
4	2.554	0.005(0.004)	0.032(0.073)	-2.287(0.229)
5	3.466	0.010(0.005)	0.029(0.073)	-2.172(0.237)
6	4.581	0.013(0.005)	0.029(0.075)	-2.129(0.240)
7	6.020	0.015(0.006)	0.028(0.075)	-2.106(0.248)
8	8.047	0.018(0.008)	0.025(0.074)	-2.051(0.267)
9	11.513	0.007(0.020)	0.025(0.073)	-2.032(0.277)
10	∞	0.010(0.035)	0.023(0.073)	-2.004(0.292)

The time dependent effects of covariates were illustrated using the breast cancer data sets using the piecewise constant hazard model. We have plotted the effects of the covariates over time for age, gender and baseline parameter.

Figure 1 shows time plots for the posterior means and ± 2 standard deviation for the intervals for the coefficients of age, gender and baseline parameter. The figure shows that the age effect increases from one interval to another. The values of the posterior mean and ± 2 standard deviation increases from one interval to another. The last interval had the widest range of values for the posterior mean and ± 2 standard deviation. The gender effect hardly changes from one interval to another and the posterior mean and ± 2 standard deviation values neither increased nor decreased. The baseline parameter also increased from one interval to another and the posterior mean and ± 2 standard deviation neither increased nor decreased. The last interval also had the widest range of values for the posterior mean and ± 2 standard deviation. The time dependent effects of all parameters will be summarised in Table 2.

Figure 1: Time plots of the posterior means and ± 2 standard deviation for the intervals for the coefficients of age, gender and baseline using the breast cancer data set



Application: Finding the Predictive Median Survival Time and Survival Probability at some Fixed Time

The MCMC samples from the practical example were thinned and 1000 samples were retained. Our procedure is used to find the survival probability at 1-year and predictive median survival time. The algorithm discussed was written using R function. The plot of the 1-year survival probability against the predictive median survival time is shown in Figure 2.

7. Discussion and Results

The usual proportional hazard model in survival model is simple to handle and is widely used in survival analysis since the hazard function is easy (Collet, 1994). This model assumes there is proportionality in the hazards and hence the covariate effects stay the same at all-time points. Here, we specify the form of the baseline hazard using a distribution. In this research, we have chosen not to use the standard proportional hazard model. We discussed the piecewise constant hazard model where the form of the dependence of the hazard function on the covariates is not specified. This has the advantage of not imposing the overall shape of the hazard function. We relaxed the proportional hazard assumption with a non-proportional hazard using the piecewise constant hazard model. We have demonstrated a Bayesian approach to using a piecewise constant hazard model with the use of a large set of data using the RJAGS software. The posterior means and standard deviation of the coefficient of all the parameters for each of the ten intervals are given in the Appendix. For instance, the posterior mean and standard deviation of the coefficient of age in the first interval (beta.age[1]) is given as 0:0013414 and 0:004746 respectively. Again, the posterior mean and standard deviation of the coefficient of address code of Eastern in the first interval (beta.addresscode[1,1]) is given as 0:1388787 and 0:173171 respectively. This follows for all other parameters in all intervals.

From Table 2, it is very obvious that covariate effects depended on time in the piecewise constant hazard model. The prognostic index in the case of the piecewise constant hazard model was not constructed in the same way as the linear predictor changes from one time interval to another and it was not obvious what the prognostic index should be in the piecewise constant hazard model. We have used the survival probability at a particular time and the predictive median survival time as an example for the prognostic index. We have computed the survival probability at 1-year and the predictive median survival time.

Table 2: A summary of the time dependent effect of all parameters using the piecewise constant hazard model

Parameter	Levels	Summary of time dependent effect
β_{Age}	nil	The covariate effect increases from one interval to another.
	1	The covariate effect slightly decreases from the first to the third interval and increases from the fourth interval to the last interval.
	2	The covariate effect slightly decreases from the first to the second interval and increases from the third interval to the last interval.
	3	The covariate effect slightly increases from the first to the fourth interval and decreases from the fifth interval to the sixth interval and later increases to the last interval.
β_{grade}	4	The covariate effect decreases from the first to the fourth interval, does not change from the fifth to the seventh interval and later increases to the last interval.
	1	The covariate effect does not change from the first to the second interval but it increases from the third interval to the last interval.
	2	The covariate effect increases from the first to the last interval.
	3	The covariate effect decreases from the first to the last interval.
$\beta_{laterality}$	4	The covariate effect decreases from the first to the fourth interval and increases from the fifth to the last interval.
	1	The covariate effect increases from the first to the last interval.
	2	The covariate effect increases from the first to the last interval.
	3	The covariate effect decreases from the first to the fourth interval and increases from the fifth to the last interval.
$\beta_{marital}$	4	The covariate effect slightly decreases from the first to the fifth interval and increases from the sixth to the last interval.
	1	The covariate effect increases from the first to the last interval.
	2	The covariate effect increases from the first to the last interval.
	3	The covariate effect increases from the first to the last interval.
	4	The covariate effect increases from the first to the last interval.
	5	The covariate effect increases from the first to the last interval.
	6	The covariate effect increases from the first to the last interval.
	7	The covariate effect slightly decreases from the first to the sixth interval and increases from the seventh to the last interval.
$\beta_{topography}$	8	The covariate effect slightly increases from the first to the third, decreases from the third to fourth interval and increases from the fifth.

	9	The covariate effect slightly decreases from the first to the seventh interval and increases from the eighth to the last interval.
	1	The covariate effect increases from one interval to another.
	2	The covariate effect increases from one interval to another.
	3	The covariate effect increases from one interval to another.
β_{extent}	4	The covariate effect decreases from one interval to another.
	1	The covariate effect increases from one interval to another.
	2	The covariate effect increases from one interval to another.
	3	The covariate effect increases from one interval to another.
	4	The covariate effect increases from one interval to another.
	5	The covariate effect increases from one interval to another.
	6	The covariate effect slightly decreases and increases from the seventh interval to the last interval.
	7	The covariate effect slightly decreases and increases from the seventh interval to the last interval.
	8	The covariate effect slightly decreases and increases from the sixth interval to the last interval.
	9	The covariate effect slightly decreases from the first to the third interval and increases from the fourth interval to the last interval.
	10	The covariate effect slightly decreases from the first to the fourth interval and increases from the fifth interval to the last interval.
	11	The covariate effect slightly decreases from the first to the fourth interval and increases from the fifth interval to the last interval.
	12	The covariate effect slightly decreases, then it increases a bit, decreases and later increase from the fifth interval to the last interval.
$\beta_{addresscode}$	13	The covariate effect slightly decreases from the first to the third interval and increases from the fourth interval to the last interval.
	14	The covariate effect slightly decreases from the first to the fourth interval and increases from the fifth interval to the last interval.

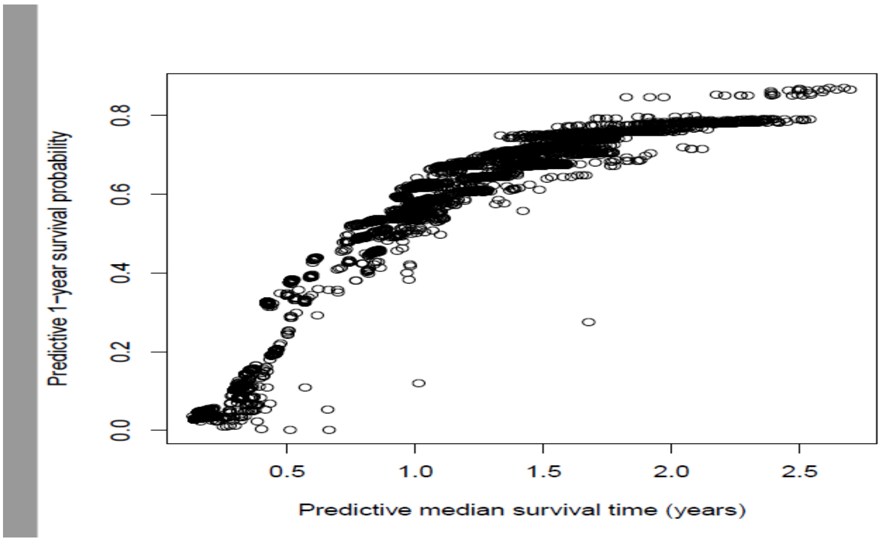


Figure 2: Plot of the survival probability at 1-year against the predictive median survival time

Figure 2 revealed that the predictive median survival time and the fixed time survival probability have a close relationship over the region where most values occur. The figure reveals some kind of patterns or clustering of points on the plot. We identified the corresponding patients by ordering the covariates by the values of either the predictive median survival time or fixed time survival probability. Further investigation revealed that the clustering was caused by discrete or categorical covariates of groups which correspond to different values of that covariate.

In this application, there may be little to be gained by calculating the predictive median survival time rather than the simpler fixed time survival probability. The fixed time survival probability appears to be just as good as an index as the predictive median survival time does. The computation of the predictive median survival time is harder than that of the fixed time survival probability. We would have the problem of the choice of time when working out the fixed time survival probability. Another problem is that the time that is most informative for one patient might be different for another patient.

Another possibility of calculating the prognostic index of a piecewise constant hazard model would be to use the survival probabilities at more than 1 time. By calculating the predictive survival probabilities at a suitable range of times, such as the cut points, we could use simple interpolation to give an approximate predictive median survival time.

8. Conclusion

This research has discussed the Bayesian methodology of relaxing the usual proportional hazard model in survival analysis by having non-proportional hazard model such as a piecewise constant hazard model with a practical application to a breast cancer data. The proportional hazard model may not be suitable if the effects of the covariates take a different form and therefore the form of dependence of the hazard function on the covariates should not be specified. We have also relaxed the form of the baseline hazard by using the piecewise constant hazard model which allows the form of the baseline hazard to change. The coefficients of the covariates also changed over time allowing for non-proportionality of hazards. The prognostic index of the piecewise constant hazard model was constructed using the survival probability at a particular time and the predictive median survival time as the prognostic index. The research showed that there is little to be gained by calculating the predictive median survival time rather than the simpler fixed time survival probability. It also shows that the fixed time survival probability appears to be just as good as an index as the predictive median survival time does.

Acknowledgements

We thank the Cancer Registry in King Faisal Specialist Hospital and Research Center (KFSH and RC) for providing the data for this study.

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Appendix

Bayesian survival modelling to Breast cancer data set using piecewise constant hazard model

	Mean	SD	Naive SE	Time-series SE
beta.addresscode[1,1]	-0.1388787	0.173171	0.0054762	0.0071431
beta.addresscode[2,1]	0.0074585	0.160132	0.0050638	0.0068116
beta.addresscode[3,1]	0.0829655	0.152131	0.0048108	0.0057054
beta.addresscode[4,1]	0.1540914	0.157568	0.0049827	0.0060117
beta.addresscode[5,1]	0.2370280	0.169740	0.0053676	0.0067539
beta.addresscode[6,1]	0.1881486	0.193010	0.0061035	0.0071573
beta.addresscode[7,1]	0.2113269	0.217408	0.0068750	0.0071423
beta.addresscode[8,1]	0.2189915	0.239912	0.0075867	0.0083881
beta.addresscode[9,1]	0.1966258	0.268335	0.0084855	0.0088806
beta.addresscode[10,1]	0.1873839	0.302256	0.0095582	0.0099443
beta.addresscode[1,2]	0.0546441	0.157023	0.0049655	0.0067188
beta.addresscode[2,2]	0.1532881	0.141256	0.0044669	0.0057701
beta.addresscode[3,2]	0.2365945	0.133605	0.0042250	0.0050052

beta.addresscode[4,2]	0.3637211	0.136109	0.0043041	0.0055543
beta.addresscode[5,2]	0.5310845	0.156872	0.0049607	0.0063588
beta.addresscode[6,2]	0.4977276	0.178611	0.0056482	0.0058755
beta.addresscode[7,2]	0.5288927	0.210328	0.0066512	0.0066491
beta.addresscode[8,2]	0.5162753	0.239563	0.0075757	0.0075734
beta.addresscode[9,2]	0.4820994	0.272739	0.0086248	0.0086235
beta.addresscode[10,2]	0.4582717	0.301280	0.0095273	0.0095202
beta.addresscode[1,3]	-0.1244004	0.225794	0.0071402	0.0089857
beta.addresscode[2,3]	-0.0197975	0.204773	0.0064755	0.0087276
beta.addresscode[3,3]	-0.0078939	0.198970	0.0062920	0.0083650
beta.addresscode[4,3]	0.0791179	0.203539	0.0064365	0.0083858
beta.addresscode[5,3]	0.1931964	0.220231	0.0069643	0.0095597
beta.addresscode[6,3]	0.1945879	0.238813	0.0075519	0.0091438
beta.addresscode[7,3]	0.2378212	0.260751	0.0082457	0.0099709
beta.addresscode[8,3]	0.2283483	0.291329	0.0092126	0.0101628
beta.addresscode[9,3]	0.2096350	0.326349	0.0103201	0.0110244
beta.addresscode[10,3]	0.1914523	0.356109	0.0112611	0.0112666
beta.addresscode[1,4]	0.0665563	0.290003	0.0091707	0.0121282
beta.addresscode[2,4]	0.1110668	0.265253	0.0083880	0.0112812
beta.addresscode[3,4]	0.1213295	0.250039	0.0079069	0.0098430
beta.addresscode[4,4]	0.1623947	0.257878	0.0081548	0.0106240
beta.addresscode[5,4]	0.2442143	0.277516	0.0087758	0.0107111
beta.addresscode[6,4]	0.2257740	0.303713	0.0096043	0.0107066
beta.addresscode[7,4]	0.2611102	0.333194	0.0105365	0.0126671
beta.addresscode[8,4]	0.2804930	0.359152	0.0113574	0.0125223
beta.addresscode[9,4]	0.2703558	0.384786	0.0121680	0.0131688
beta.addresscode[10,4]	0.2513915	0.405524	0.0128238	0.0140009
beta.addresscode[1,5]	0.0267810	0.266741	0.0084351	0.0098597
beta.addresscode[2,5]	0.0933760	0.227181	0.0071841	0.0083963
beta.addresscode[3,5]	0.1523572	0.220716	0.0069797	0.0077640
beta.addresscode[4,5]	0.0972812	0.239122	0.0075617	0.0075624
beta.addresscode[5,5]	0.1231575	0.265606	0.0083992	0.0088030
beta.addresscode[6,5]	0.0539334	0.296216	0.0093672	0.0097301
beta.addresscode[7,5]	0.0512529	0.327517	0.0103570	0.0108086
beta.addresscode[8,5]	0.0454133	0.362127	0.0114515	0.0114497
beta.addresscode[9,5]	0.0359587	0.406397	0.0128514	0.0128485
beta.addresscode[10,5]	0.0309325	0.434214	0.0137311	0.0137309
beta.addresscode[1,6]	0.0876169	0.258248	0.0081665	0.0102052
beta.addresscode[2,6]	0.1436333	0.228478	0.0072251	0.0083460
beta.addresscode[3,6]	0.0498035	0.210818	0.0066666	0.0081555
beta.addresscode[4,6]	0.0681618	0.230767	0.0072975	0.0075914
beta.addresscode[5,6]	0.0091003	0.265731	0.0084032	0.0087427
beta.addresscode[6,6]	-0.1549345	0.305547	0.0096623	0.0096643
beta.addresscode[7,6]	-0.2011545	0.351201	0.0111059	0.0114864
beta.addresscode[8,6]	-0.1330252	0.392908	0.0124248	0.0124272
beta.addresscode[9,6]	-0.1198397	0.441304	0.0139553	0.0139622
beta.addresscode[10,6]	-0.1055134	0.484137	0.0153098	0.0146793
beta.addresscode[1,7]	-0.0100189	0.210800	0.0066661	0.0088422
beta.addresscode[2,7]	-0.2104280	0.182194	0.0057615	0.0075185

beta.addresscode[3,7]	-0.3929164	0.163837	0.0051810	0.0060986
beta.addresscode[4,7]	-0.3621626	0.170669	0.0053970	0.0060848
beta.addresscode[5,7]	-0.3458817	0.224494	0.0070991	0.0083585
beta.addresscode[6,7]	-0.4140807	0.258191	0.0081647	0.0088456
beta.addresscode[7,7]	-0.3301904	0.293995	0.0092969	0.0098131
beta.addresscode[8,7]	-0.3129593	0.358068	0.0113231	0.0113216
beta.addresscode[9,7]	-0.3128081	0.433407	0.0137055	0.0137101
beta.addresscode[10,7]	-0.3078504	0.489164	0.0154687	0.0154725
beta.addresscode[1,8]	0.1640573	0.340903	0.0107803	0.0119217
beta.addresscode[2,8]	0.1532036	0.303323	0.0095919	0.0100526
beta.addresscode[3,8]	0.3326927	0.305789	0.0096699	0.0111201
beta.addresscode[4,8]	0.1226030	0.329236	0.0104114	0.0115458
beta.addresscode[5,8]	0.0509316	0.339393	0.0107326	0.0115179
beta.addresscode[6,8]	0.0328602	0.385367	0.0121864	0.0127066
beta.addresscode[7,8]	-0.0837871	0.447268	0.0141439	0.0145814
beta.addresscode[8,8]	-0.1093396	0.500737	0.0158347	0.0158426
beta.addresscode[9,8]	-0.0860935	0.567030	0.0179311	0.0179375
beta.addresscode[10,8]	-0.0782145	0.617587	0.0195298	0.0195385
beta.addresscode[1,9]	-0.1451539	0.437750	0.0138429	0.0156977
beta.addresscode[2,9]	-0.1678542	0.397738	0.0125776	0.0140604
beta.addresscode[3,9]	-0.1906462	0.381076	0.0120507	0.0114155
beta.addresscode[4,9]	-0.1816178	0.416436	0.0131689	0.0131509
beta.addresscode[5,9]	-0.1403321	0.446732	0.0141269	0.0150707
beta.addresscode[6,9]	0.0615861	0.507835	0.0160591	0.0157863
beta.addresscode[7,9]	0.0879648	0.566442	0.0179125	0.0180860
beta.addresscode[8,9]	0.1824346	0.644940	0.0203948	0.0198923
beta.addresscode[9,9]	0.1649959	0.700475	0.0221510	0.0211319
beta.addresscode[10,9]	0.1635220	0.754321	0.0238537	0.0231467
beta.addresscode[1,10]	-0.8316370	0.535076	0.0169206	0.0219432
beta.addresscode[2,10]	-0.8438706	0.456580	0.0144383	0.0200267
beta.addresscode[3,10]	-0.7409190	0.422393	0.0133572	0.0172396
beta.addresscode[4,10]	-0.6980758	0.416691	0.0131769	0.0166169
beta.addresscode[5,10]	-0.4914104	0.463170	0.0146467	0.0166492
beta.addresscode[6,10]	-0.3963019	0.534078	0.0168890	0.0188875
beta.addresscode[7,10]	-0.4027342	0.632051	0.0199872	0.0207513
beta.addresscode[8,10]	-0.3869783	0.720567	0.0227863	0.0227723
beta.addresscode[9,10]	-0.3707570	0.791297	0.0250230	0.0239700
beta.addresscode[10,10]	-0.3543279	0.839025	0.0265323	0.0265448
beta.addresscode[1,11]	-0.1135328	0.558361	0.0176569	0.0190743
beta.addresscode[2,11]	-0.1082260	0.498495	0.0157638	0.0189811
beta.addresscode[3,11]	-0.2049782	0.466562	0.0147540	0.0166184
beta.addresscode[4,11]	-0.1967426	0.475574	0.0150390	0.0156106
beta.addresscode[5,11]	0.0978771	0.494972	0.0156524	0.0176558
beta.addresscode[6,11]	0.3285546	0.574098	0.0181546	0.0181570
beta.addresscode[7,11]	0.2975811	0.694665	0.0219672	0.0219791
beta.addresscode[8,11]	0.2716535	0.785982	0.0248549	0.0242298
beta.addresscode[9,11]	0.2551333	0.869134	0.0274844	0.0285707
beta.addresscode[10,11]	0.2300766	0.926200	0.0292890	0.0292559
beta.addresscode[1,12]	-0.0337704	0.402148	0.0127170	0.0138424

beta.addresscode[2,12]	-0.2238490	0.370318	0.0117105	0.0112177
beta.addresscode[3,12]	-0.0510147	0.352162	0.0111363	0.0111764
beta.addresscode[4,12]	0.0443791	0.370996	0.0117319	0.0117223
beta.addresscode[5,12]	-0.4782787	0.421521	0.0133297	0.0133347
beta.addresscode[6,12]	-0.5477230	0.480306	0.0151886	0.0151868
beta.addresscode[7,12]	-0.5796450	0.564815	0.0178610	0.0178407
beta.addresscode[8,12]	-0.6439707	0.674513	0.0213300	0.0213122
beta.addresscode[9,12]	-0.5978761	0.768669	0.0243075	0.0242971
beta.addresscode[10,12]	-0.5532891	0.867962	0.0274474	0.0264238
beta.addresscode[1,13]	0.9733997	0.901793	0.0285172	0.0420207
beta.addresscode[2,13]	0.8680100	0.854641	0.0270261	0.0434461
beta.addresscode[3,13]	0.6851857	0.835214	0.0264118	0.0416341
beta.addresscode[4,13]	0.6743923	0.869178	0.0274858	0.0399126
beta.addresscode[5,13]	0.5217093	0.950892	0.0300699	0.0413284
beta.addresscode[6,13]	0.5092500	1.017881	0.0321882	0.0436825
beta.addresscode[7,13]	0.4966140	1.079259	0.0341292	0.0420565
beta.addresscode[8,13]	0.4403287	1.137770	0.0359795	0.0425523
beta.addresscode[9,13]	0.4219285	1.203672	0.0380635	0.0437140
beta.addresscode[10,13]	0.3950842	1.276538	0.0403677	0.0458673
beta.addresscode[1,14]	0.0243369	0.539976	0.0170755	0.0177005
beta.addresscode[2,14]	0.0439889	0.448021	0.0141677	0.0146797
beta.addresscode[3,14]	-0.0725603	0.438762	0.0138749	0.0147662
beta.addresscode[4,14]	-0.3275437	0.542995	0.0171710	0.0193777
beta.addresscode[5,14]	-0.5523960	0.689951	0.0218182	0.0226791
beta.addresscode[6,14]	-0.5793822	0.806890	0.0255161	0.0261262
beta.addresscode[7,14]	-0.5750527	0.927998	0.0293459	0.0291943
beta.addresscode[8,14]	-0.5976651	1.004833	0.0317756	0.0321842
beta.addresscode[9,14]	-0.5493580	1.096528	0.0346753	0.0327749
beta.addresscode[10,14]	-0.5089194	1.178068	0.0372538	0.0387636
beta.age[1]	-0.0013414	0.004746	0.0001501	0.0004170
beta.age[2]	0.0005447	0.004085	0.0001292	0.0003244
beta.age[3]	0.0021059	0.003954	0.0001250	0.0002515
beta.age[4]	0.0047631	0.004076	0.0001289	0.0002573
beta.age[5]	0.0096648	0.004518	0.0001429	0.0002672
beta.age[6]	0.0128863	0.005118	0.0001618	0.0002515
beta.age[7]	0.0154237	0.005659	0.0001790	0.0001987
beta.age[8]	0.0176215	0.007847	0.0002481	0.0002779
beta.age[9]	0.0072945	0.019580	0.0006192	0.0006193
beta.age[10]	0.0099934	0.034576	0.0010934	0.0012291
beta.extent[1,1]	0.0010218	0.087969	0.0027818	0.0033829
beta.extent[2,1]	0.0295219	0.081280	0.0025703	0.0029045
beta.extent[3,1]	0.0779282	0.076162	0.0024085	0.0024698
beta.extent[4,1]	0.1232842	0.079567	0.0025161	0.0027675
beta.extent[5,1]	0.1312550	0.082186	0.0025989	0.0029428
beta.extent[6,1]	0.1370954	0.088704	0.0028051	0.0029986
beta.extent[7,1]	0.1536889	0.098226	0.0031062	0.0032837
beta.extent[8,1]	0.1624159	0.109592	0.0034656	0.0034664
beta.extent[9,1]	0.1512074	0.118824	0.0037575	0.0037570
beta.extent[10,1]	0.1447897	0.126017	0.0039850	0.0039865

beta.extent[1,2]	-0.6712354	0.085363	0.0026994	0.0033438
beta.extent[2,2]	-0.6775765	0.076590	0.0024220	0.0030117
beta.extent[3,2]	-0.6484582	0.072910	0.0023056	0.0028859
beta.extent[4,2]	-0.6075181	0.076259	0.0024115	0.0026708
beta.extent[5,2]	-0.5949473	0.080853	0.0025568	0.0027539
beta.extent[6,2]	-0.5712705	0.085966	0.0027185	0.0033174
beta.extent[7,2]	-0.5259759	0.094638	0.0029927	0.0034651
beta.extent[8,2]	-0.4885455	0.106810	0.0033776	0.0039904
beta.extent[9,2]	-0.4673144	0.116461	0.0036828	0.0042644
beta.extent[10,2]	-0.4418281	0.126520	0.0040009	0.0040025
beta.extent[1,3]	-0.5933682	0.101398	0.0032065	0.0034712
beta.extent[2,3]	-0.5632609	0.086776	0.0027441	0.0030951
beta.extent[3,3]	-0.4859316	0.078097	0.0024696	0.0030225
beta.extent[4,3]	-0.4306283	0.082762	0.0026172	0.0029444
beta.extent[5,3]	-0.4004642	0.089963	0.0028449	0.0028463
beta.extent[6,3]	-0.3881110	0.104533	0.0033056	0.0028704
beta.extent[7,3]	-0.4096079	0.112300	0.0035512	0.0034046
beta.extent[8,3]	-0.3833231	0.127760	0.0040401	0.0041997
beta.extent[9,3]	-0.3592701	0.149306	0.0047215	0.0056461
beta.extent[10,3]	-0.3406102	0.163635	0.0051746	0.0051771
beta.extent[1,4]	1.2635818	0.100247	0.0031701	0.0038069
beta.extent[2,4]	1.2113156	0.086485	0.0027349	0.0029410
beta.extent[3,4]	1.0564616	0.082023	0.0025938	0.0027279
beta.extent[4,4]	0.9148621	0.086912	0.0027484	0.0027493
beta.extent[5,4]	0.8641565	0.101332	0.0032044	0.0032058
beta.extent[6,4]	0.8222860	0.119158	0.0037681	0.0035299
beta.extent[7,4]	0.7818949	0.141144	0.0044634	0.0044616
beta.extent[8,4]	0.7094527	0.162288	0.0051320	0.0049508
beta.extent[9,4]	0.6753771	0.186928	0.0059112	0.0059054
beta.extent[10,4]	0.6376485	0.203366	0.0064310	0.0061782
beta.gender[1,1]	0.0397935	0.074491	0.0023556	0.0042961
beta.gender[2,1]	0.0402296	0.072323	0.0022870	0.0042737
beta.gender[3,1]	0.0338277	0.073155	0.0023134	0.0042529
beta.gender[4,1]	0.0316361	0.072542	0.0022940	0.0042575
beta.gender[5,1]	0.0292317	0.073437	0.0023223	0.0042465
beta.gender[6,1]	0.0289367	0.074823	0.0023661	0.0041686
beta.gender[7,1]	0.0279906	0.074828	0.0023663	0.0040758
beta.gender[8,1]	0.0251260	0.074290	0.0023493	0.0039044
beta.gender[9,1]	0.0249088	0.073489	0.0023239	0.0037062
beta.gender[10,1]	0.0234899	0.073330	0.0023189	0.0033322
beta.gender[1,2]	-0.0397935	0.074491	0.0023556	0.0042961
beta.gender[2,2]	-0.0402296	0.072323	0.0022870	0.0042737
beta.gender[3,2]	-0.0338277	0.073155	0.0023134	0.0042529
beta.gender[4,2]	-0.0316361	0.072542	0.0022940	0.0042575
beta.gender[5,2]	-0.0292317	0.073437	0.0023223	0.0042465
beta.gender[6,2]	-0.0289367	0.074823	0.0023661	0.0041686
beta.gender[7,2]	-0.0279906	0.074828	0.0023663	0.0040758
beta.gender[8,2]	-0.0251260	0.074290	0.0023493	0.0039044
beta.gender[9,2]	-0.0249088	0.073489	0.0023239	0.0037062

beta.gender[10,2]	-0.0234899	0.073330	0.0023189	0.0033322
beta.grade[1,1]	-0.2353660	0.126795	0.0040096	0.0058082
beta.grade[2,1]	-0.2784930	0.122734	0.0038812	0.0057588
beta.grade[3,1]	-0.2829944	0.121273	0.0038350	0.0056434
beta.grade[4,1]	-0.2833719	0.124654	0.0039419	0.0058270
beta.grade[5,1]	-0.2368768	0.129338	0.0040900	0.0060016
beta.grade[6,1]	-0.1983779	0.133123	0.0042097	0.0057666
beta.grade[7,1]	-0.1645298	0.138528	0.0043806	0.0056891
beta.grade[8,1]	-0.1544105	0.144414	0.0045668	0.0055795
beta.grade[9,1]	-0.1487081	0.147951	0.0046786	0.0054841
beta.grade[10,1]	-0.1395728	0.154028	0.0048708	0.0054888
beta.grade[1,2]	-0.2081482	0.099740	0.0031541	0.0042683
beta.grade[2,2]	-0.2466335	0.088444	0.0027968	0.0037093
beta.grade[3,2]	-0.2310527	0.086807	0.0027451	0.0035162
beta.grade[4,2]	-0.2181315	0.087774	0.0027756	0.0034690
beta.grade[5,2]	-0.1557738	0.092467	0.0029241	0.0035787
beta.grade[6,2]	-0.1047730	0.098897	0.0031274	0.0033226
beta.grade[7,2]	-0.0652010	0.105563	0.0033382	0.0038073
beta.grade[8,2]	-0.0629814	0.117359	0.0037112	0.0039427
beta.grade[9,2]	-0.0622002	0.126192	0.0039905	0.0042735
beta.grade[10,2]	-0.0591828	0.133557	0.0042234	0.0044210
beta.grade[1,3]	0.1253516	0.108735	0.0034385	0.0053198
beta.grade[2,3]	0.2293232	0.096084	0.0030384	0.0039555
beta.grade[3,3]	0.3125323	0.091634	0.0028977	0.0037512
beta.grade[4,3]	0.3402717	0.096375	0.0030476	0.0040531
beta.grade[5,3]	0.2557130	0.102021	0.0032262	0.0036285
beta.grade[6,3]	0.2187085	0.114444	0.0036190	0.0041201
beta.grade[7,3]	0.1699319	0.125267	0.0039613	0.0043752
beta.grade[8,3]	0.1709397	0.143029	0.0045230	0.0048452
beta.grade[9,3]	0.1608893	0.157962	0.0049952	0.0049977
beta.grade[10,3]	0.1555038	0.169357	0.0053555	0.0053582
beta.grade[1,4]	0.3181626	0.208440	0.0065914	0.0096375
beta.grade[2,4]	0.2958033	0.190594	0.0060271	0.0082861
beta.grade[3,4]	0.2015147	0.191370	0.0060516	0.0083693
beta.grade[4,4]	0.1612317	0.199612	0.0063123	0.0077244
beta.grade[5,4]	0.1369376	0.212894	0.0067323	0.0087377
beta.grade[6,4]	0.0844424	0.226639	0.0071669	0.0086853
beta.grade[7,4]	0.0597989	0.241645	0.0076415	0.0088724
beta.grade[8,4]	0.0464521	0.263964	0.0083473	0.0094954
beta.grade[9,4]	0.0500190	0.277476	0.0087746	0.0096483
beta.grade[10,4]	0.0432518	0.288644	0.0091277	0.0097051
beta.laterality[1,1]	-0.2495105	0.130312	0.0041208	0.0082731
beta.laterality[2,1]	-0.2428431	0.124752	0.0039450	0.0088027
beta.laterality[3,1]	-0.1594059	0.125822	0.0039788	0.0085883
beta.laterality[4,1]	-0.1134526	0.129235	0.0040868	0.0082105
beta.laterality[5,1]	-0.1291303	0.135745	0.0042926	0.0082215
beta.laterality[6,1]	-0.1358347	0.142448	0.0045046	0.0085422
beta.laterality[7,1]	-0.1474188	0.150508	0.0047595	0.0082073
beta.laterality[8,1]	-0.1536882	0.159557	0.0050456	0.0082693

beta.laterality[9,1]	-0.1468693	0.163793	0.0051796	0.0070804
beta.laterality[10,1]	-0.1380165	0.170657	0.0053966	0.0071623
beta.laterality[1,2]	-0.2765250	0.130058	0.0041128	0.0084125
beta.laterality[2,2]	-0.2297913	0.124106	0.0039246	0.0078906
beta.laterality[3,2]	-0.1522917	0.126291	0.0039937	0.0085027
beta.laterality[4,2]	-0.1173832	0.131826	0.0041687	0.0083057
beta.laterality[5,2]	-0.0637956	0.140000	0.0044272	0.0089583
beta.laterality[6,2]	-0.0527721	0.141818	0.0044847	0.0087445
beta.laterality[7,2]	-0.0541878	0.145254	0.0045933	0.0086146
beta.laterality[8,2]	-0.0511182	0.154778	0.0048945	0.0083896
beta.laterality[9,2]	-0.0518135	0.163310	0.0051643	0.0077492
beta.laterality[10,2]	-0.0499827	0.171159	0.0054125	0.0077547
beta.laterality[1,3]	0.3668749	0.259656	0.0082110	0.0206046
beta.laterality[2,3]	0.3722881	0.257621	0.0081467	0.0188783
beta.laterality[3,3]	0.3352949	0.259783	0.0082151	0.0194783
beta.laterality[4,3]	0.3124166	0.259269	0.0081988	0.0207574
beta.laterality[5,3]	0.2841004	0.269227	0.0085137	0.0190821
beta.laterality[6,3]	0.2600197	0.273457	0.0086475	0.0186846
beta.laterality[7,3]	0.2476780	0.275380	0.0087083	0.0173652
beta.laterality[8,3]	0.2259779	0.277793	0.0087846	0.0163858
beta.laterality[9,3]	0.2139686	0.278113	0.0087947	0.0163170
beta.laterality[10,3]	0.2028336	0.280618	0.0088739	0.0150026
beta.laterality[1,4]	0.1591606	0.212814	0.0067298	0.0093205
beta.laterality[2,4]	0.1003462	0.199912	0.0063218	0.0093360
beta.laterality[3,4]	-0.0235972	0.201032	0.0063572	0.0094377
beta.laterality[4,4]	-0.0815808	0.215113	0.0068025	0.0096471
beta.laterality[5,4]	-0.0911745	0.230008	0.0072735	0.0095073
beta.laterality[6,4]	-0.0714130	0.237245	0.0075023	0.0093556
beta.laterality[7,4]	-0.0460714	0.248131	0.0078466	0.0083049
beta.laterality[8,4]	-0.0211716	0.264033	0.0083495	0.0097931
beta.laterality[9,4]	-0.0152858	0.280235	0.0088618	0.0100077
beta.laterality[10,4]	-0.0148345	0.282525	0.0089342	0.0100892
beta.marital[1,1]	-0.2634098	0.087496	0.0027669	0.0033423
beta.marital[2,1]	-0.2444237	0.078048	0.0024681	0.0030856
beta.marital[3,1]	-0.1983179	0.077863	0.0024623	0.0029105
beta.marital[4,1]	-0.1433568	0.082545	0.0026103	0.0030310
beta.marital[5,1]	-0.0931767	0.088659	0.0028036	0.0030181
beta.marital[6,1]	-0.0781723	0.099145	0.0031352	0.0034185
beta.marital[7,1]	-0.0764298	0.106582	0.0033704	0.0037454
beta.marital[8,1]	-0.0636185	0.117547	0.0037172	0.0037173
beta.marital[9,1]	-0.0578880	0.129291	0.0040885	0.0040890
beta.marital[10,1]	-0.0526976	0.140343	0.0044380	0.0046100
beta.marital[1,2]	-0.1835432	0.118404	0.0037443	0.0056496
beta.marital[2,2]	-0.1958192	0.116016	0.0036687	0.0060648
beta.marital[3,2]	-0.1843658	0.116900	0.0036967	0.0056926
beta.marital[4,2]	-0.1691559	0.118269	0.0037400	0.0056317
beta.marital[5,2]	-0.1473760	0.120826	0.0038209	0.0051557
beta.marital[6,2]	-0.1445858	0.125944	0.0039827	0.0056200
beta.marital[7,2]	-0.1407793	0.132508	0.0041903	0.0057952

beta.marital[8,2]	-0.1286698	0.142073	0.0044928	0.0057941
beta.marital[9,2]	-0.1214703	0.147682	0.0046701	0.0055393
beta.marital[10,2]	-0.1138464	0.155008	0.0049018	0.0059676
beta.marital[1,3]	-0.1144417	0.133364	0.0042173	0.0053959
beta.marital[2,3]	-0.1330813	0.122133	0.0038622	0.0056834
beta.marital[3,3]	-0.1758167	0.118775	0.0037560	0.0047368
beta.marital[4,3]	-0.1818544	0.120202	0.0038011	0.0052928
beta.marital[5,3]	-0.1921584	0.130175	0.0041165	0.0049808
beta.marital[6,3]	-0.1862384	0.137014	0.0043328	0.0055132
beta.marital[7,3]	-0.1762422	0.148986	0.0047114	0.0056097
beta.marital[8,3]	-0.1704588	0.160874	0.0050873	0.0056679
beta.marital[9,3]	-0.1627422	0.173409	0.0054837	0.0057984
beta.marital[10,3]	-0.1582058	0.184876	0.0058463	0.0058461
beta.marital[1,4]	0.5613947	0.173366	0.0054823	0.0057249
beta.marital[2,4]	0.5733242	0.157974	0.0049956	0.0056821
beta.marital[3,4]	0.5585004	0.154714	0.0048925	0.0057445
beta.marital[4,4]	0.4943672	0.166363	0.0052609	0.0059555
beta.marital[5,4]	0.4327111	0.184613	0.0058380	0.0060395
beta.marital[6,4]	0.4089965	0.205881	0.0065105	0.0068249
beta.marital[7,4]	0.3934513	0.224734	0.0071067	0.0079928
beta.marital[8,4]	0.3627471	0.246600	0.0077982	0.0078673
beta.marital[9,4]	0.3421006	0.267104	0.0084466	0.0084351
beta.marital[10,4]	0.3247498	0.283271	0.0089578	0.0093240
beta.topography[1,1]	0.1167945	0.193992	0.0061346	0.0071339
beta.topography[2,1]	0.1283809	0.181868	0.0057512	0.0066680
beta.topography[3,1]	0.1320673	0.175004	0.0055341	0.0063670
beta.topography[4,1]	0.1671191	0.171621	0.0054271	0.0060847
beta.topography[5,1]	0.2172810	0.180212	0.0056988	0.0062286
beta.topography[6,1]	0.3096278	0.187213	0.0059202	0.0063522
beta.topography[7,1]	0.3417614	0.200210	0.0063312	0.0067987
beta.topography[8,1]	0.3297924	0.216384	0.0068427	0.0065476
beta.topography[9,1]	0.3183744	0.231486	0.0073202	0.0076165
beta.topography[10,1]	0.2965737	0.249071	0.0078763	0.0079806
beta.topography[1,2]	-0.1192688	0.181892	0.0057519	0.0066236
beta.topography[2,2]	-0.1266221	0.167075	0.0052834	0.0063759
beta.topography[3,2]	-0.1347699	0.165010	0.0052181	0.0059604
beta.topography[4,2]	-0.1004747	0.170442	0.0053899	0.0063598
beta.topography[5,2]	-0.0624031	0.170462	0.0053905	0.0062436
beta.topography[6,2]	0.0304575	0.185620	0.0058698	0.0067428
beta.topography[7,2]	0.0740941	0.199224	0.0063000	0.0070988
beta.topography[8,2]	0.0793235	0.213081	0.0067382	0.0074880
beta.topography[9,2]	0.0770278	0.235487	0.0074467	0.0076867
beta.topography[10,2]	0.0658183	0.254304	0.0080418	0.0086908
beta.topography[1,3]	-0.1075315	0.200443	0.0063386	0.0072819
beta.topography[2,3]	-0.0971923	0.179544	0.0056777	0.0066318
beta.topography[3,3]	-0.0714606	0.167747	0.0053046	0.0065569
beta.topography[4,3]	0.0257207	0.169662	0.0053652	0.0063940
beta.topography[5,3]	0.1142364	0.174784	0.0055272	0.0062150
beta.topography[6,3]	0.2026358	0.190009	0.0060086	0.0062816

beta.topography[7,3]	0.2570610	0.206031	0.0065153	0.0069293
beta.topography[8,3]	0.2741668	0.225903	0.0071437	0.0074465
beta.topography[9,3]	0.2580550	0.251990	0.0079686	0.0079726
beta.topography[10,3]	0.2350739	0.270817	0.0085640	0.0085663
beta.topography[1,4]	0.0420882	0.239850	0.0075847	0.0087657
beta.topography[2,4]	0.0650266	0.218148	0.0068984	0.0082476
beta.topography[3,4]	0.0309812	0.206154	0.0065192	0.0073800
beta.topography[4,4]	0.1654183	0.208083	0.0065802	0.0067678
beta.topography[5,4]	0.2433705	0.224282	0.0070924	0.0073746
beta.topography[6,4]	0.3762708	0.248870	0.0078700	0.0075446
beta.topography[7,4]	0.3861999	0.276864	0.0087552	0.0084133
beta.topography[8,4]	0.3744960	0.308476	0.0097549	0.0094507
beta.topography[9,4]	0.3626771	0.332391	0.0105111	0.0105021
beta.topography[10,4]	0.3460391	0.345385	0.0109220	0.0105309
beta.topography[1,5]	-0.3244190	0.176654	0.0055863	0.0071398
beta.topography[2,5]	-0.2895488	0.150748	0.0047671	0.0073533
beta.topography[3,5]	-0.2346310	0.142905	0.0045191	0.0054798
beta.topography[4,5]	-0.0756505	0.146298	0.0046264	0.0053920
beta.topography[5,5]	-0.1064567	0.159093	0.0050310	0.0058983
beta.topography[6,5]	-0.1021209	0.172485	0.0054545	0.0058597
beta.topography[7,5]	-0.0949587	0.195137	0.0061708	0.0061716
beta.topography[8,5]	0.0221647	0.228792	0.0072350	0.0072386
beta.topography[9,5]	0.0410552	0.281319	0.0088961	0.0087773
beta.topography[10,5]	0.0391079	0.330547	0.0104528	0.0096136
beta.topography[1,6]	-0.5590985	0.291299	0.0092117	0.0115465
beta.topography[2,6]	-0.6084117	0.254469	0.0080470	0.0098932
beta.topography[3,6]	-0.5274739	0.228889	0.0072381	0.0086558
beta.topography[4,6]	-0.4650865	0.233310	0.0073779	0.0083879
beta.topography[5,6]	-0.3658653	0.252420	0.0079822	0.0083653
beta.topography[6,6]	-0.4156445	0.274581	0.0086830	0.0086361
beta.topography[7,6]	-0.3756128	0.297272	0.0094006	0.0088793
beta.topography[8,6]	-0.3911952	0.344506	0.0108942	0.0108502
beta.topography[9,6]	-0.3707703	0.393481	0.0124430	0.0124161
beta.topography[10,6]	-0.3524991	0.433793	0.0137177	0.0137015
beta.topography[1,7]	0.5776328	0.425628	0.0134596	0.0158152
beta.topography[2,7]	0.4597472	0.416932	0.0131846	0.0176346
beta.topography[3,7]	0.1928777	0.417936	0.0132163	0.0187585
beta.topography[4,7]	-0.0393017	0.434001	0.0137243	0.0185373
beta.topography[5,7]	-0.1856353	0.431697	0.0136514	0.0163404
beta.topography[6,7]	-0.2802707	0.441522	0.0139622	0.0180889
beta.topography[7,7]	-0.3270540	0.467149	0.0147725	0.0186270
beta.topography[8,7]	-0.3508685	0.498817	0.0157740	0.0176684
beta.topography[9,7]	-0.3295804	0.538426	0.0170265	0.0156255
beta.topography[10,7]	-0.3160499	0.571576	0.0180748	0.0191133
beta.topography[1,8]	-0.0333645	0.204692	0.0064729	0.0082598
beta.topography[2,8]	-0.0293007	0.182578	0.0057736	0.0065872
beta.topography[3,8]	0.1499521	0.155020	0.0049022	0.0056117
beta.topography[4,8]	-0.0994061	0.172943	0.0054689	0.0057250
beta.topography[5,8]	-0.1068467	0.189546	0.0059940	0.0067366

beta.topography[6,8]	-0.2334878	0.222641	0.0070405	0.0076383
beta.topography[7,8]	-0.2312527	0.250140	0.0079101	0.0069353
beta.topography[8,8]	-0.3000323	0.324344	0.0102567	0.0096503
beta.topography[9,8]	-0.2970485	0.419093	0.0132529	0.0132380
beta.topography[10,8]	-0.2723058	0.505258	0.0159777	0.0167435
beta.topography[1,9]	0.4071669	0.170244	0.0053836	0.0075683
beta.topography[2,9]	0.4979210	0.139410	0.0044085	0.0054938
beta.topography[3,9]	0.4624571	0.133525	0.0042224	0.0053430
beta.topography[4,9]	0.4216615	0.151304	0.0047847	0.0053603
beta.topography[5,9]	0.2523192	0.180111	0.0056956	0.0056951
beta.topography[6,9]	0.1125320	0.205032	0.0064837	0.0063935
beta.topography[7,9]	-0.0302383	0.248360	0.0078538	0.0078578
beta.topography[8,9]	-0.0378475	0.335095	0.0105966	0.0106009
beta.topography[9,9]	-0.0597902	0.472951	0.0149560	0.0146094
beta.topography[10,9]	-0.0417581	0.572299	0.0180977	0.0166138
beta0[1]	-2.8004833	0.237707	0.0075170	0.0250800
beta0[2]	-2.6927998	0.228519	0.0072264	0.0250930
beta0[3]	-2.4443389	0.224229	0.0070907	0.0260313
beta0[4]	-2.2869011	0.228754	0.0072338	0.0231701
beta0[5]	-2.1715219	0.236681	0.0074845	0.0218532
beta0[6]	-2.1291042	0.239917	0.0075868	0.0225320
beta0[7]	-2.1061894	0.247784	0.0078356	0.0196670
beta0[8]	-2.0513336	0.266818	0.0084375	0.0178815
beta0[9]	-2.0322993	0.277243	0.0087672	0.0192463
beta0[10]	-2.0035495	0.292100	0.0092370	0.0175141