Bayesian Estimation of parameters for Survival models using the Cox Proportional model

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Abstract

The main objective of the study was to predict the mortality of people in African countries. Using data from the DHS and functions from the **mortDHS** package, functions were created to support the data from any given country within the set of DHS surveys, a useful model is generated to make survival predictions and evaluate the effects associated with covariables and, using the posterior distributions, test significance and similarities between these covariables, these probabilistic interpretations can not be done using non-parametric models as Kaplan-Meier, which was the first model proposed. Specifically, a discrimination is obtained between the differences in the survival of each person depending on their sex and country, these predictions are made from a Bayesian approach using the **rstanarm** package, which uses the Stan software to make its estimates.

Introduction

The problem

In our study we were interested in estimating the mortality on African countries. These countries sometimes lack of a good and reliable registry of deaths and without these estimating mortality rates can be difficult, these rates have prime importance on epidemiological or socio-economic studies.

In our study we used the survey data provided by DHS, these contain a large number of variables, people were asked about the survival status of their siblings so we only include sibling data on our study, we assess siblings survival, expecting to derivate from these the mortality of the population.

Study Population

Many countries don't have good registries management on government institutions and thus they don't have a good record of important events such as population deaths, the Demographic and Health Surveys (DHS) facilitates multiple datasets containing data collected from questionnaires performed in households from a large list of countries.

In our study we will consider the Individual Women's data, which consist of questionnaires performed to women. They were asked about wherever they had siblings, their survival status, age and death date (in case they have died).

Data source

The primary data source was the Demographic and Health Surveys (DHS) Individual Recode (IR) where each row consist of a woman and their responses on multiple questions. There were multiple columns but we selected the ones related to siblings and their survival status, these where:

- Sibling sex (male or female)
- Sibling date of birth
- Sibling survival status (0 = dead, 1 = alive)
- Sibling date of death
- Sibling country of residency
    - On particular, we only selected the data from countries Malawi, Senegal and Rwanda. But the functions can be extended to any set of countries.

From these we calculated the variable **time**, which has a great importance on survival analysis in general.

Basic concepts

Survival analysis

Survival analysis is a collection of statistical methods for study the time that elapses until an event occurs [1]. The name survival is due to the fact that the applications of this method are mainly study the times of death, some fields of the application of survival analysis They include: medicine, epidemiology, economics, among others. An advantage of models based on survival analysis is that they allow work with censored data, censoring occurs when you have some information on the survival time of a patient but the exact time to failure is not known.

There are three functions of interest for survival analysis, the survival function denoted $S(t)$, the hazard function denoted $h(t)$, and the hazard function accumulated denoted by $H(t)$, these will be the amounts of interest for our study. According to the literature [2], functions are defined as follows:

Let T be a random variable denoting the survival time of a unit or person. The survival function, which is denoted $S(t)$ gives the probability that a unit or person will survives beyond some specific time t. i.e,

$$S(t) = P(T > t)$$

The survival function $S(t)$ is fundamental in AS since for different values of t provide crucial information of survival data In some situations it may be more interest to quantify the risk of failure at a given instant than to estimate survival; a function of interest in survival analysis that allows do this is the danger function

The hazard function usually denoted as $h(t)$ or $\lambda(t)$ is given by:

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t \leq T + \Delta t | T \geq t)}{\Delta t}$$

The numerator represents the conditional probability of the event occurring in an infinitesimal interval $[t, t+\Delta t]$ (as $\Delta t \to 0$) given that the unit has survived to t ($T > t$). survived until t (T>t).

The cumulative hazard is defined as:

$$H(t) = \int_0^t h(s)ds$$

Where $h(s)$ is the hazard function. exist a one to-one relationship between the hazard function, the cumulative hazard and the probability of survival, as follows

$$S(t) = exp(-H(t)) = exp(-\int_0^t h(s)ds)$$

Censorship

An observation in a random variable T is said to be right-censored if all that is known about of T is that it is greater than some value c. In AS, T refers at the time of occurrence of some particular event and a case is considered right-censored if it stops observing before for the event to occur[3]. In our work, only the right caesura is presented, since at the time of conducting the survey there were people who had not yet experienced the event of interest (death).

Survival probability can be estimated nonparametrically over temporal observations (censored and uncensored) using the Kaplan-Meyer method. other two Common approaches to modeling survival data consist of modeling the instantaneous rate of the event as a function of time. This includes the class of models known as proportional hazards regression models and non-proportional hazards regression models; the second is to model the time of the event itself. This includes the class of models known as accelerated time to failure (AFT) models.

Bayesian approach and why Bayesian

The main reason to go Bayesian in our study was to be able to make inference, in particular, to make easy to interpretative conclusions on our parameters and their significance, without the assumptions of frecuentists approaches.

Models

Under this modeling framework, it is proposed to implement a of Bayesian Cox proportional hazard to later make a comparison versus the frequentest approach and the Kaplan-Meier estimation.

Kaplan–Meier estimator

The Kaplan-Meier estimator, also known as the limit product estimator, is a nonparametric method for es-

timating the survival function. survival function by maximizing the sample likelihood function. Suppose one has k different failure times $t_1 < t_2 < ... < t_k$, in each time $t_j (j = 1, 2, ...k)$ there are n_j subjects that are under observation and at risk of an event of interest.

The K-M estimator is defined as

$$\hat{S}_{KM}(t) = \prod_{j:t_j \leq t} [1 - \frac{d_j}{n_j}]$$

$$para \quad t_1 \leq t \leq t_k \quad y \quad d_j = \#faults$$

Cox proportional hazards model

Under a hazard scale formulation, we model the hazard of the event for individual i at time t using the following model:

$$h(t|X_i) = h_0(t)exp(X_i\beta)$$

Where h_0 is called the hazard base, that is, $h_0(t)$ is the risk when all X_i variables are 0. $h_0(t)$ characterizes the way in which hazard changes as a function of survival time, while the second term characterizes the way the hazard changes as function of the covariates at the same time guarantees that this is positive, it is also called the linear predictor.

The formulation of the Cox model in terms of the hazard and the survival function are given by: From (2) we note that

$$S(t; x) = exp(-H(t; x))$$

Where $H(t; \vec{x})$ is the cumulative hazard for a subject with covariates $\vec{x} = (x_1, x_2, ..x_k)$ Assuming survival time is continuous

$$H(t; \vec{x}) = \int_0^t h(s; \vec{x})ds = \int_0^t h_0(s)exp(\beta^T \vec{x})ds$$

$$= exp(\beta^T \vec{x}) \int_0^t h_0(s)ds = exp(\beta^T \vec{x})H_0(T)$$

Cox model in terms of cumulative hazard. In this expression $H_0(t)$ is the cumulative baseline hazard. This relationship can be thought of as a baseline cumulative risk measure which is modified according to the function

From the above relationship, the Cox model can be formulated in terms of survival:

$$S(t; \vec{x}) = exp(-H(t; \vec{x})) = exp(e^{\beta^T \vec{x}})H_0(t) =$$

$$[exp(-H_0(t)]^{e^{\beta^T \vec{x}}} = [S_0(t)]^{e^{\beta^T \vec{x}}}$$

Cox model in terms of survival. In this expression $S_0(t)$ is the survival baseline.

Estimation

As we previously seen, the cox proportional hazard model has two parts, one is the baseline hazard and the second one is the linear model, for the linear model we only choose to estimate each of the β using normal prios, but for the hazard baseline

Linear Model

From the Cox Proportional-Hazards Model we can extract the following expression, which we call the linear model.

$$\exp(\beta \cdot X_i)$$

Where $\beta = (\beta_0, \beta_1, ..., \beta_n)$ is the vector of coefficients and $X_i = (1, x_1, ..., x_n)$ is the vector of covariables.

On our study the will have vector $X_i = (1, \mathrm{I}_{\text{sex = female}}, \mathrm{I}_{\text{country = Rwanda}}, \mathrm{I}_{\text{country = Senegal}})$, that is because we have two variables and both of them are factors, the indicator for the *male* sex and the country *Malawi* are the reference represented by the intercept β_0.

For this particular model we set our priors as such:

$$\beta_0 \sim N(0, 20)$$

$$\beta_i \sim N(0, 2.5) \quad \text{with i = 1, 2, 3}$$

Baseline Hazard

In our study we used an M-Spline model to approximate the hazard baseline function h_0, this approximation consists of γ_l coefficients multiplied by each component of the spline, function calculated inside by the package **splines2**.

So the hazard of dying for the individual i at time t is given by:

$$h_i(t) = \exp(\beta \cdot X_i) * \sum_{l=1}^{L} \gamma_l \mathrm{M}_l(t \mid k, \delta)$$

Where $k = \{k_1, ..., k_J\}$ is a set of knots given by the user, we observed that a decent number of knots is around 6 (including the 2 boundary knots, k_1 located at the earliest entry time and k_J, located at the lastest event), this number of knots prevents that our model is too overfitting, We will leave the default degree of the splines δ at 3.

The package **rstanarm** handles the calculation and sets a Dirichlet prior with concentration parameter of 1, ensuring an non-informative prior.

Model Selection

To evaluate the performance of the predictions of each model we use a cross-validation technique. Through the loo() function that is included in the *rstanarm* package. The way this package divides the data in the cross validation is leaving a single observation out, the unit that is systematically omitted determines the predictive task in which the cross-validation evaluates the performance of the model, the computational method implemented is Pareto-smoothed importance sampling.

the Pareto- $\hat{k}$ diagnostic estimates how far an individual leave-one-out distribution is from the full distribution. If leaving out an observation changes the posterior too much then importance sampling is not able to give reliable estimate. If $\hat{k} < 0.5$, then the corresponding component of elpd_loo is estimated with high accuracy. If $0.5 < \hat{k} < 0.7$ the accuracy is lower, but still OK. if $\hat{k} > 0.7$, then importance sampling is not able to provide useful estimate for that component/observation.

The p_loo is called the effective number of parameters and can be calculated as the difference between the pd_loo and the log posterior predictive density without cross-validation. In well behaving cases p_loo$< N$ and p_loo $< p$, where p is the total number of parameters in the model. p_loo $> N$ or p_loo $> p$ indicates that the model has very weak predictive capability.

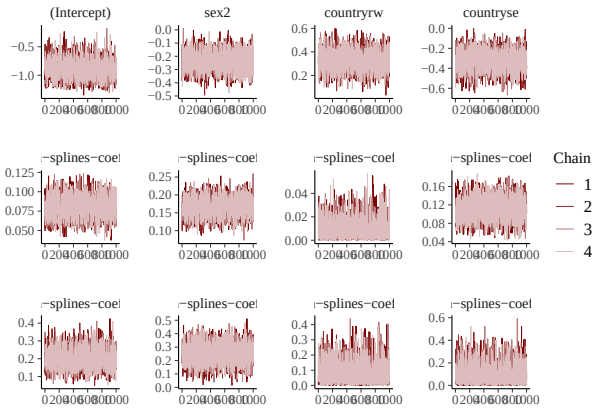
Evaluating the predictive capacity of each model, it was obtained that the best performance is given by the model that specifies the hazard baseline as a spline, so our work will be developed based on this model, these results are attached in the annex.

Results

Convergence of estimation

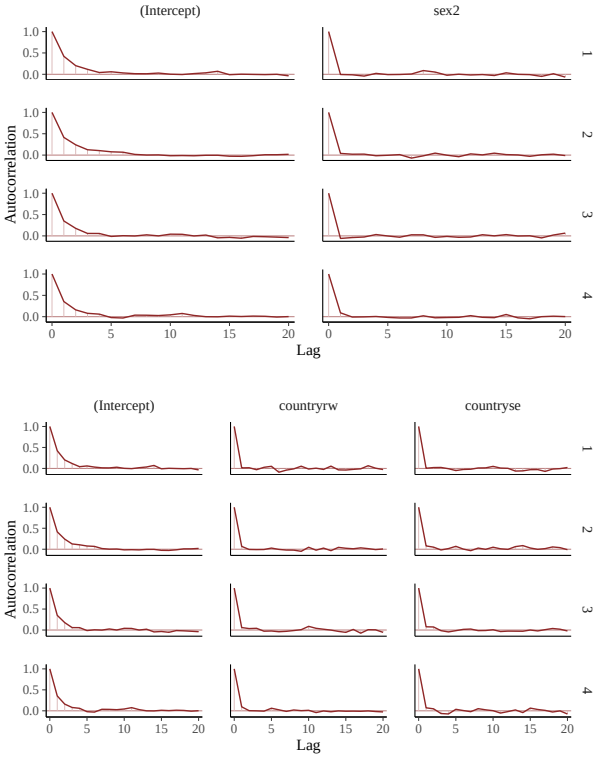
Traceplot

As we can see in the following graph, we achieved a nice convergence for each of the 3 chains.



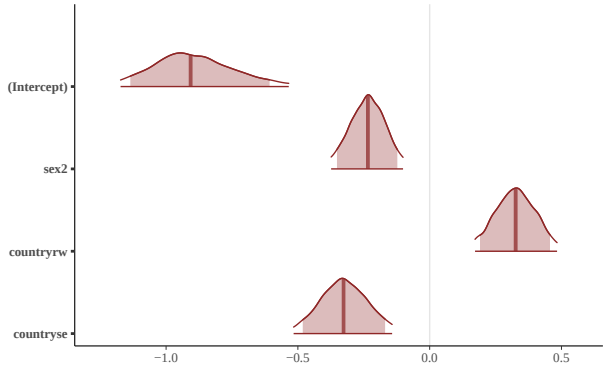
Autocorrelation

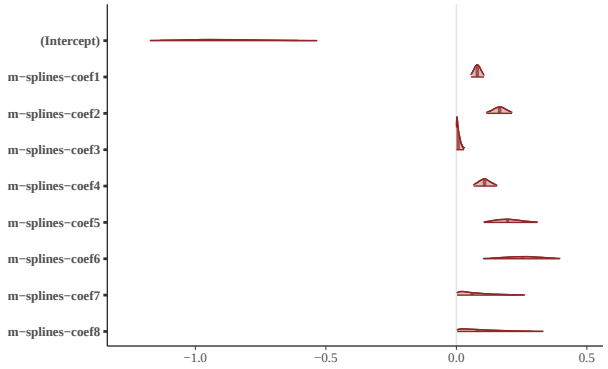
In the following graphs we check for autocorrelation between each of the coefficients estimated, as we can see we had a good convergence.



Estimate

In the following graphs we can see posterior probabilities distributions for estimated parameters, as we can see none of them contains 0, that means that all of them have different effects on survival.





	mean	sd	10%	50%
Intercept	-0.891	0.161	-1.087	-0.907
sex2	-0.235	0.069	-0.327	-0.234
countryrw	0.326	0.080	0.224	0.326
countryse	-0.326	0.095	-0.446	-0.327

Table 1: parameter estimation bayesian approach

	coef	exp(coef)	se(coef)
sex2	-0.23247	0.79257	0.06862
countryrw	0.32528	1.38441	0.08013
countryse	-0.33077	0.71837	0.09340

Table 2: parameter estimation frequentist approach

Annexes

	mcse	Rhat	n_eff
Intercept	0.004	1.002	1432
sex2	0.001	1.000	3866
countryrw	0.001	1.001	3419
countryse	0.002	1.001	3404

Table 3: MCMC diagnostics

	Estimate	SE
elpd_loo	-7089.7	197.5
p_loo	8.3	0.3
looic	14179.5	395.1
Monte Carlo SE of elpd_loo is 0.0.		
All Pareto k estimates are good (k <0.5)		

Table 4: loo splines

	Estimate	SE
elpd_loo	-7429.6	205.2
p_loo	4.2	0.1
looic	14859.1	410.4
Monte Carlo SE of elpd_loo is 0.0.		
All Pareto k estimates are good (k <0.5)		

Table 5: loo exponential

	Estimate	SE
elpd_loo	-7187.3	199.7
p_loo	4.8	0.1
looic	14374.7	399.4
Monte Carlo SE of elpd_loo is 0.0.		
All Pareto k estimates are good (k <0.5)		

Table 6: loo Weibull

	elpd_diff	se_diff
mod_spline	0.0	0.0
mod_weibull	-97.6	12.0
mod_exp	-339.8	31.2

Table 7: loo compare

References

[1] Allison, PD. (1995). Survival Analysis Using the SAS System: A practical guide, Cary, NC:SAS Institute Inc., 292 pp.

[2] COX, D. R. Regression Models and Life Tables (with Discussion), Journal of The Royal Statistical Society, Series B, 34, 187-220, 1972.

[3] ALLISON, P.D. Discrete-Time Methods for the Analysis of Event Histories, In Sociological Methodology 1982, ed. S. Leinhardt, San Francisco, CA: Jossey-Bass, 1982.