Detection of Multiple Change Points in an Accelerated Failure Time Model Using Sequential Testing

Kayoung Park and Kristine Gierz Old Dominion University

Abstract

With improvements to cancer diagnoses and treatments, incidences and mortality rates have changed. However, the most commonly used analysis methods do not account for such distributional changes. In survival analysis, change point problems can concern a shift in a distribution for a set of time-ordered observations, potentially under censoring or truncation. We propose a sequential testing approach for detecting multiple change points in the Weibull accelerated failure time model, since this is sufficiently flexible to accommodate increasing, decreasing, or constant hazard rates and is also the only continuous distribution for which the accelerated failure time model can be reparametrized as a proportional hazards model. Our sequential testing procedure does not require the number of change points to be known; this information is instead inferred from the data. We conduct a simulation study to show that the method accurately detects change points and estimates the model. The numerical results along with a real data application demonstrate that our proposed method can detect change points in the hazard rate.

Proposed Method

Using the Weibull AFT model, we propose a model that has a change point in the scale parameter:

$$\lambda(t_i) = \begin{cases} \lambda_1 & \text{if} \quad 0 < t_i \le \tau_1 \\ \lambda_2 & \text{if} \quad \tau_1 < t_i \le \tau_2 \\ \vdots & \\ \lambda_{k+1} & \text{if} \quad t_i > \tau_k \end{cases}$$

- $0 = \tau_0 < \tau_1 < \cdots < \tau_k < \infty$: the change points
- k: the number of change points
- α: the shape parameter
- $\boldsymbol{\beta}$: the vector of regression coefficients
- $\boldsymbol{Z_i}$: the covariate vector for i^{th} patient
- $\boldsymbol{\theta} = (\boldsymbol{\beta}, \alpha, \lambda_1, \cdots, \lambda_{k+1}, \tau_1, \cdots, \tau_k)$
- The hazard function for the change point model:

$$h(t_i; \boldsymbol{Z_i}) = \alpha \lambda_j t_i^{\alpha-1} \exp(\boldsymbol{\beta}' \boldsymbol{Z_i}) I(\tau_{j-1} < t_i \le \tau_j)$$

- The likelihood function of the Weibull AFT change point model with $\boldsymbol{\theta}$:

$$L(\boldsymbol{\theta}) = \prod_{i=1}^{N} \left[f(t_i; \boldsymbol{Z_i})\right]^{\delta_i} \left[S(t_i; \boldsymbol{Z_i})\right]^{1-\delta_i}$$

Because the number of change points is assumed to be unknown, we propose a sequential testing procedure to determine the number of change points in the Weibull AFT model using an alpha spending function.

- In step m $(m = 0, 1, 2, \cdots)$,

$$H_{0,m} : k = m \quad \text{versus} \quad H_{1,m} : k = m + 1$$

- $\boldsymbol{\theta}_{0,m}$ and $\boldsymbol{\theta}_{1,m}$: the vector of unknown parameters in the null and alternative models in step m, respectively.
- The likelihood ratio test statistic at step m:

$$LR_m = -2\left[\sup l(\boldsymbol{\theta}_{0,m}) - \sup l(\boldsymbol{\theta}_{1,m})\right]$$

- For the overall significance level $\boldsymbol{\alpha}$, we want $\alpha^*(m) = \boldsymbol{\alpha}/2^m$, where $\alpha^*(m)$ is the significance level in step m. Therefore, $\alpha^*(1) > \alpha^*(2) > \cdots > \alpha^*(K)$.

Due to known issues with the distribution of LR_m, we use a bootstrap procedure to estimate empirical distribution:

- Calculate the cumulative hazard estimate $\widehat{H}(t_i)$ using the maximum likelihood estimates $\widehat{\boldsymbol{\theta}}_{0,m}$ and the Kaplan–Meier estimate $\widehat{S}_c(t_i)$ for the survival function of the censoring variable C_i. The estimated survival function for the observed time is given by $\widehat{S}_{H_{0,m}}(t_i) = \exp\left\{\widehat{H}(t_i)\right\}$.
- Generate B simulated datasets based on $\widehat{S}_{H_{0,m}}$ corresponding to a true model under the null, and the censoring distribution $\widehat{S}_c(t_i)$. Calculate the likelihood ratio statistic $LR_m^b, b = 1, \ldots, B$ for each resampled trial.
- Reject the null hypothesis if LR_m, the likelihood ratio statistic calculated from the data, is larger that the $(1 - \alpha^*(m)) \times 100^{th}$ percentile of $\left\{LR_m^b, b = 1, \ldots, B\right\}$.

Simulation Study

We conducted an extensive simulation study under several different sample sizes and censoring rates, and found that our method accurately estimates the model with a reasonable power and Type I error.

Sample size	Censoring rate	Parameters	Constant Hazard Model		Proposed Model	
			MEAN	MSE	MEAN	MSE
500	0%	$\tau_1 = 2.00$	$1.998^\dagger$	$0.001^\dagger$	2.006	0.002
		$\tau_2 = 4.00$	$10.242^\dagger$	$62.442^\dagger$	4.072	0.370
	20%	$\tau_1 = 2.50$	2.496	0.007	2.520	0.002
		$\tau_2 = 6.00$	12.129	48.489	6.001	0.616

Table 1: Averaged point estimates and MSE values of the estimated parameters of the proposed model and piecewise constant hazard model of Goodman et al. (2011) based on 1000 replicated simulations for the two-change point model with two continuous covariates. The † denotes a convergence issue for the piecewise constant hazard method and that the simulated trials that had this issue were removed from the calculations.

Sample size	Censoring rate	True Model	Detected Model			
			0 changes	1 change	2 changes	3 changes
500	0%	0 changes	0.945	0.045	0.010	0.000
		1 change	0.005	0.948	0.047	0.000
		2 changes	0.000	0.004	0.933	0.063
	20%	0 changes	0.920	0.080	0.000	0.000
		1 change	0.006	0.909	0.086	0.000
		2 changes	0.000	0.150	0.810	0.040

Table 2: Power and Type I error results for the sequential hypothesis testing.

Real Data Analysis

To examine prostate cancer mortality, we use Surveillance, Epidemiology, and End Results program (www.seer.cancer.gov) data.

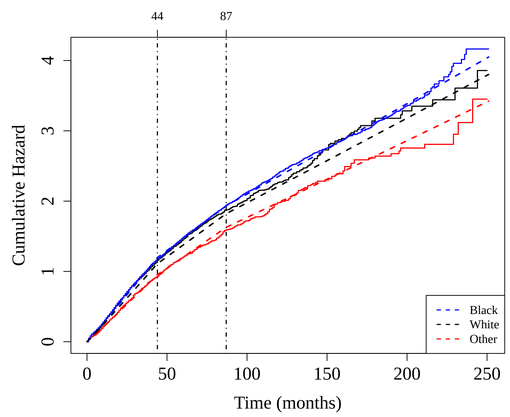

Figure 1: The Nelson–Aalen estimates by race are the solid lines, while the dashed lines represent the proposed method. The vertical dotted lines represent the location of the change point estimates for the proposed method.

Conclusion

- In this study, we present a sequential testing procedure to determine the number of change points in the Weibull AFT model using an alpha spending function and select a parsimonious model rather than an over-fitted one.
- The numerical examples show that our proposed method is more flexible and accurate in estimating the values of the parameters than other models, making it effective in handling cases with possible change points.

Future Research

- To obtain accurate and reliable results, it is necessary to evaluate the validity of the assumptions of the our proposed model and check the adequacy of the model fit. However, in practice, the required assumptions of the model might not be met. It is therefore important to generalize our method to such a case as well.