A self-starting Risk-adjusted AFT-based control chart for monitoring the survival time of patients

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Abstract

Since the processes in the health-care domain deal with humans' life, the slightest deviation from the normal state can lead to irreparable damages to individuals and society. Therefore, monitoring the quality of the processes in this area has attracted many researchers' attention. On the other hand, the introduction of new therapies for various diseases has made process monitoring difficult due to the lack of historical data. In this paper, the effect of heterogeneity of patient conditions (including gender, age, etc.) and treatment in different conditions (such as treatment with different therapist groups) has been considered using the accelerated failure time (AFT) regression model and the risk of each patient has been adjusted accordingly. Then, survival times of patients are monitored using a control chart based on the residual values of the AFT regression. Performance of the proposed control chart is evaluated using the average run length (ARL) criterion. The results indicate that the proposed method has a proper performance in identifying out-of-control status in processes in the health-care domain. The results showed that taking into account the therapist groups as well as increasing the number of in-control observations, increase the ability of the proposed control chart to detect shifts in the process.

Keywords
Accelerated failure time, Average run length, Censoring, Risk adjustment, Self-starting control chart, Survival data

1. Introduction

Due to the competitive environment and efforts to maximize profits, quality plays a crucial role in the success of today's organizations. Therefore, organizations need to improve the quality of their products and services by minimizing errors, and they use different quality control tools to do so, including control charts. In organizations related to the health-care field, issues beyond the profit should be considered. Because of the high cost of therapy mistakes, the use of quality tools in this area has been increased, and hospitals and health-care centers have consistently sought ways to identify system errors and to remove their effects.

The first and most important step in monitoring processes in SPC is to identify the appropriate quality characteristics for monitoring by using the control chart. Various factors such as the rate of infection in the surgery department, the mortality rate after treatment, the survival time after treatment, the duration of admission and the waiting time in the admission can be considered as quality characteristics in health-care systems (Benneyan, 1998a, 1998b).

The survival time of patients after treatment is one of the most important criterion which is studied in this paper.

This measure defines as the time to especial event such as death, infection, tumor growth and recovery in medical applications.

In survival analysis, not considering the difference between the health conditions of patients referring to the organization can lead to an incorrect interpretation of the process. to tackle this problem, risk-adjusted (RA) control charts are used to consider this factor (Grigg and Farewell, 2004; Iezzoni, 2013). RA models have been developed over the past 20 years in health-care processes, for example, surgery, mental health, home care and general care in the hospital are some of the fields in which risk adjustment has been used to monitor the quality of processes. Heart surgery is one of the most common areas for RA studies(Steiner, 2000; Paynabar et al., 2012; Asadayyoobi and Niaki, 2017) due to complete reports of the patients' condition and the high risk of this operation.

Various tools based on parametric or non-parametric models have been used to adjust the effect of risk factors. Accelerated failure time (AFT) regression (Sego et al., 2009; Steiner and Jones, 2010; Asadayyoobi and Niaki, 2017) and cox model (Biswas and Kalbfleisch, 2008) are the most widely used tools in the parametric models.

The lack of adequate information from the patient's survival after the treatment process is also common in survival data from a common health domain, which uses the concept of censored data to consider this challenge. On the other hand, in many cases, new therapies are provided for the treatment of diseases in which full historical data is not available from them, and it is not possible to perform the Phases I and II of SPC separately for them (Zeng and Zhou, 2011). In these cases, self-starting control charts should be used for monitoring purpose. (Aminnayeri and Sogandi, 2016) proposed a self-starting scheme based on a parametric bootstrap method and dynamic probability control limits for the risk-adjusted Bernoulli cumulative sum control charts, but they use binary survival data, which has less information about the monitoring process.

Given the above issues, in this paper, the process associated with a new therapeutic approach, where historical data is not available, is monitored based on the continuous survival times by considering the patient's health state and the therapist's group in hearth surgery. To this end, the AFT model is used for risk adjustment of patients and then, survival times of patients are monitored using a control chart based on the residual values of the AFT regression model.

The remainder of the paper is structured as follows: In Section 2, the proposed method is explained. Simulation study and the results have been reported in Section 3 and conclusion and a recommendation for future research is given in Section 4.

2. Proposed method

The self-starting control charts are presented by Hawkins (Hawkins, 1987) for simultaneous implementation of Phases I and II. These charts are used if there is not sufficient historical data to estimate the parameters or when it is essential to update the estimated values for parameters. In self-starting control chart initially, the parameters are estimated using a small number of data, called 'reference value', and when a new observation is added, if the observation is detected in the in-control state, the parameters are updated based on new data and the control limits are reviewed. Otherwise, the process is detected as out-of-control. AFT regression is used to estimate the coefficients which are used to adjust the risk of each patient and consider therapist groups. Unlike the products in manufacturing processes that are relatively homogeneous, Patients vary in many respects, which ignoring this leads to inaccurate conclusion from the process. Therefore, risk factors must be considered in the model for a fair conclusion. To do so, AFT regression model has been used in this paper for Weibull distribution. Weibull distribution has a high degree of flexibility to model survival time. This distribution can have constant, decreasing or increasing failure rates, depending on the values of the parameters.

Censoring is one of the characteristics of the survival time data. Censoring occurs when events do not occur within a given study time period. There are various categories of censoring data, including right censored data, left-censored data, and interval censored data. In this paper, right censored data is used in statistical modeling, defined as below.

$$T_i = \min(x_i, c), \tag{1}$$

$$d_i = \begin{cases} 1 & if\ x_i \leq c \\ 0 & if\ x_i > c' \end{cases} \tag{2}$$

In this equations, x_i is the actual survival time of patient i, c is the period of study and d_i is the indicator of censoring. If one covariate considered in the model, The AFT regression model for the Weibull distribution is defined as follows:

$$Y_i = \log(T_i) = \beta_0 + \beta_1 z_1 + \sigma\epsilon_i, \tag{3}$$

In this Equation, ε_i is the random error value for patient i and follows extreme value distribution. The values of the regression coefficient of β_0, β_1 and σ must be estimated based on maximum likelihood method. The likelihood function is defined for pairs of (T_i, d_i)as follows:

$$L(T_i, d_i) = \prod_{i=1}^{n} \Pr(T_i, d_i) = \prod_{i=1}^{n} [f(t_i)]^{d_i} [S(t_i)]^{1-d_i}, \tag{4}$$

where $f(.)$ and $S(.)$ are the density and survival functions of extreme value distribution. To consider the effect of therapists in AFT model, the logarithm of T_i for patients is written as:

$$Log(T_i) = \beta_0 + \beta_1 Z_i + \sum_{i=1}^{n-1} \gamma_i f_{ij} + \sigma\varepsilon_i, \quad (5)$$

where f_{ij} is the dummy variables and γ_i is the regression coefficient for each dummy variable.
Given that the random error and $Log(T_i)$ have a linear relationship with each other, the standardized residual value for patient *i* will be equal to:

$$e_i = \frac{Y_i - \hat{\beta}_0 - \hat{\beta}_1 z_i}{\hat{\sigma}}. \quad (6)$$

It has been shown that the standardized residual value has as the same distribution as random error (Lindqvist, Kvaløy and Aaserud, 2015). Hence, e_i follows extreme value distribution. Accordingly, in the proposed method, after obtaining e_i for each patient, the cumulative probability distribution $F_{ev}(e_i)$ is calculated and a value of normal distribution (ZN_i) is obtained that the probability of its cumulative distribution is equal to the obtained value $F_{ev}(e_i)$.

$$ZN_i = \phi^{-1}\left(F_{ev}(e_i)\right), \quad (7)$$

In this equation, $F_{ev}(.)$ is the cumulative probability function for the standardized residual of the patient i and ZN_i is the inverse normal distribution value with the probability of a cumulative distribution equal to the obtained value $F_{ev}(e_i)$. In order to increase the chart's ability to detect small shifts, ZN_i statistic will be written in one-way EWMA, based on the below equation.

$$Z_i = min\{\lambda \times ZN_i + (1-\lambda) \times Z_{i-1}, 0\}, \quad (8)$$

where λ is the smoothing coefficient and is considered equal to 0.2. If the survival time of a patient is greater than the estimated value, the value is zero and otherwise, it will have a negative value. The lower control limit of the proposed statistic is calculated by using simulation such that a desired ARL_0 is obtained.

3. Simulation study

The proposed method is capable of performing on a variety of processes in the healthcare field, however, in this paper, it is used to monitor the survival time of patients with Cardiac surgery. In this surgery patients are monitored for 30 days, so *c* can be considered 30 in this process. The Parssonet score (Parsonnet, Dean and Bernstein, 1989) has been used to consider the patients' health status in Equation (3) as the value for z_1. This score has an integer that ranges from 0 to 100 based on the patients' gender, age, blood pressure, etc. Another factor that affects the quality of treatment is the difference in therapist groups. Differences in the expertise and capabilities of therapist groups can lead to different outcomes for patients with same Parssonet scores. The Cardiac surgery in Stiener (Steiner, 2000) has been used to simulate data in this paper. Also, it is supposed that there are three therapist groups in the process, for who two dummy variables f_{i1} and f_{i2} are defined.

Simulation studies have been used to evaluate the performance of proposed methods. In order to obtain suitable results in all simulations, all simulations have been implemented with 5000 iterations. As stated before, the ARL criterion was used to evaluate the performance of the proposed method in detecting out-of-control status. At the beginning of the simulation, $\hat{\beta}$ and $\hat{\gamma}$ values are estimated based on 10 reference values, and in next steps, decisions are made to stop the process or to update the regression coefficients of the risk factors based on in-control or out-of-control state of the process. Note that LCL is set by 5000 simulation runs to achieve ARL_0 equals to 200. In order to simulate shifts in the process, negative shifts in regression coefficients are considered and the ability of the proposed control chart to detect the shift is measured in terms of ARL_1 accordingly.

In order to illustrate the effect of considering the therapist groups in the results of the simulated model, the results are reported in two parts. In the first part, AFT risk adjustment is modeled only by considering the effect of Parsonnet score and the results of the change in the parameters β_0 and β_1 are reported for different values. Then, the effect of considering the therapist groups on the performance of control chart is evaluated and compared with the previous results.

The results obtained for different shifts in β_0 and β_1 for changes at observations 20, 40 and 80, with and without considering therapist groups are reported in Tables 1 to Table 6. The reported values are the difference between the time of receiving out-of-control alarm and the real time of the change in the process.

Table 1. The ARL_1values based on the change at $t = 20$ without considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL_1	5.63	11.90	21.92	31.46	35.96	41.23	46.55	50.44	52.62
	std(ARL_1)	0.22	0.36	0.50	0.54	0.56	0.58	0.60	0.62	0.63
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL_1	2.01	2.09	2.24	2.68	3.85	12.15	34.97	42.86	49.17
	std(ARL_1)	0.01	0.01	0.01	0.02	0.10	0.35	0.58	0.59	0.61

Table 2.The ARL_1 values based on the change at *t*=40 without considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL_1	4.91	8.70	17.21	27.66	32.44	37.83	45.91	50.53	51.86
	std(ARL_1)	0.15	0.24	0.37	0.46	0.48	0.52	0.54	0.55	0.56
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL_1	2.02	2.09	2.24	2.67	3.63	9.38	29.12	40.92	49.24
	std(ARL_1)	0.01	0.01	0.01	0.02	0.06	0.24	0.47	0.53	0.56

Table 3. The ARL_1 values based on the change at *t*=80 without considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL_1	3.93	7.54	13.64	22.13	27.53	32.19	37.92	40.67	42.14
	std(ARL_1)	0.07	0.15	0.25	0.33	0.36	0.39	0.40	0.42	0.42
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL_1	2.03	2.11	2.24	2.67	3.41	7.99	23.29	34.87	40.26
	std(ARL_1)	0.01	0.01	0.01	0.02	0.03	0.15	0.34	0.40	0.42

Table 4. The ARL_1values based on the change at *t*=20 with considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL_1	5.06	10.14	19.08	27.57	31.54	36.30	43.36	46.83	47.70
	std(ARL_1)	0.18	0.32	0.46	0.52	0.51	0.54	.58	.59	.6
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL_1	2.01	2.05	2.24	2.64	3.54	10.27	31.58	39.50	46.58
	std(ARL_1)	0.01	0.01	0.01	0.02	0.06	0.32	0.55	0.57	.54

Table 5. The ARL_1 values based on the change at *t*=40 with considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL_1	4.25	8.33	15.69	26.07	29.69	35.36	42.15	46.48	49.30
	std(ARL_1)	0.12	0.23	0.36	0.45	.46	.5	.53	.54	.56
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL_1	2.00	2.09	2.24	2.64	3.41	8.76	27.01	39.69	45.50
	std(ARL_1)	0.01	0.01	0.01	0.02	0.04	0.22	.44	.53	.54

Table 6. The ARL_1 values based on the change at t=80 with considering the therapist groups

β_0	Shift	-5	-4	-3	-2	-1.5	-1	-0.5	-0.25	-0.1
	ARL1	4.02	7.36	13.05	21.04	25.84	31.97	37.25	40.08	44.14
	std(ARL1)	0.08	0.15	.25	.32	.36	.39	.41	.44	.47
β_1	Shift	-0.5	-0.4	-0.3	-0.2	-0.15	-0.1	-0.05	-0.03	-0.01
	ARL1	2.02	2.10	2.21	2.65	3.31	7.36	23.17	33.20	40.18
	std(ARL1)	0.01	0.01	.01	.02	.03	.14	.33	.4	.44

Results indicate that by increasing the size of the shift in the regression coefficients, the ARL_1 decreases, which is reasonable because by increasing the size of the shift, the control chart will require few observations until receiving out-of-control alarm. Furthermore, the ARL_1 will decrease when the regression coefficients have been estimated with more in-control data. Considering the effect of therapist groups in the AFT regression model leads to decreasing in the ARL_1 values, which suggests that considering the effect of therapists in the proposed risk-adjusted model leads to better performance of the proposed control chart.

4. Conclusion and suggestion for future research

In this paper, considering the residuals of the AFT risk-adjusted model as a statistic, a self-starting control chart was proposed to monitor the process in the field of health-care. The results show that the proposed method has an acceptable performance in identifying shifts in the process especially when the regression coefficients have been estimated with more in-control data. More researches should be done on the monitoring of self-starting control charts especially with continuous survival data. For example, investigating the other distributions rather than Weibull or developing a self-starting control based on likelihood ratio test can be fruitful area for future research.

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