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Nonparametric estimate of conditional quantile residual lifetime for right censored data

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A nonparametric approach is proposed to estimate the quantile residual lifetime at a given time while considering the effect of covariates. An estimating equation is constructed and a local Kaplan-Meier estimator is employed to incorporate the covariates in the equation while leaving the distribution of survival time unspecified. Asymptotic properties including both consistency and asymptotic normality of the proposed estimator are established and a resampling method is proposed to estimate the asymptotic variance. Simulation studies are conducted to assess the finite-sample performance of the estimator, and an HIV survival data is analyzed using the proposed method.

Keywords and phrases: Local Kaplan-Meier estimate, Quantile residual lifetime, Right censored data.

1. INTRODUCTION

Residual lifetime has attracted more and more attention in recent years. It is defined as the remaining time of life provided that individual has survived over some time and it has been studied by investigators in various fields. In study of survival in HIV patients, for example, both patient and doctor wish to know how much one's lifetime could be left after one had already survived two years since one's initial diagnosis. Residual lifetime is such an index that is very revealing about the information of the remaining life. And it is important to make statistical inference for residual lifetime.

There are two well-known existing measurements related to residual lifetime. One is the Kaplan-Meier(Kaplan and Meier 1958) estimate of the survival function, which provides the probability that a patient will survive beyond any given specified time. For example, by referring to the Kaplan-Meier plot, physicians can tell the probability of the HIV patient who has survived over 2 years since initial diagnosis. However, if the patient wants to know more information, such as the longevity of the rest of lifetime, given that one has survived over 2 years since the diagnosis, physicians will fail to make an answer directly from the plot. Furthermore, it is difficult to estimate residual life time by the Kaplan-Meier method when the residual life time of an individual depends on some covariates or the environmental backgrounds. Another measurement is the hazard function, which is defined as conditioning on that subject has survived over some time t, the instantaneous failure rate of the subject at the following moment. The higher value of hazard function shows a higher risk of failure. And the most frequently used hazard function is the Cox proportional hazards model (Cox 1972, 1975), which assumes a form of a baseline hazard function, multiplied by an exponential function specifying the effect of covariates on the failure risk. Whereas the model assumption is often challenged and questioned. Moreover, the Cox model which describes "instantaneous rate of failure" is conceptually difficult to understand and it is not easy to explain when the residual life time needs to be evaluated in the middle of an observation period. Thus, it is better to estimate residual time directly.

Several ways have been proposed to characterize the residual lifetime directly, including mean, median and quantile residual lifetime. To study the mean residual lifetime, both nonparametric methods (Yang 1977; Chaubey and Sen 1999, 2008; Abdous and Berred 2005; McLain and Ghosh 2011) and semi-parametric models (Oakes and Dasu 1990, 2003; Maguluri and Zhang 1994; Chen and Cheng 2005, 2006; Chen et al. 2005; Sun, Song and Zhang 2012) have been investigated by many authors. The semi-parametric models, such as proportional mean residual lifetime model, additive expectancy regression model and semi-parametric transformation model, are convenient to consider the effects of covariates; however, it is difficult to judge which one of these models fits the real data. Meanwhile, mean residual life function has a one-to-one relationship with the survival function and there needs some restrictions to ensure this correspondence. Moreover, it is not robust enough when the distribution of residual lifetime is highly skewed or heavy-tailed.

Median residual lifetime, by contrast, is a more robust way to assess the remaining lifetime and less restrictive than the model based on the mean residual, because it doesn't uniquely determine the survival function (Gupta and Langford 1984). Besides median, we can offer a more complete analysis of the remaining lifetime by modelling a broad range of quantiles of the residual lifetime, i.e., quantile residual lifetime, which has been extensively studied in

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recent contexts. For example, without considering the effects of covariates, Jeong, Jung and Costantino (2008) proposed a nonparametric estimation for the median residual life function by using the Kaplan-Meier estimator, which can be easily extended to the quantiles residual lifetime. To compare two quantile residual life functions, Franco-Pereira, Lillo and Romo (2012) presented a nonparametric method for constructing confidence bands for the difference of two quantile residual life functions, and Jeong and Fine (2013) proposed a two-sample test statistic and associated confidence interval for inference on the ratio of two cause-specific quantile residual life functions under competing risks. Sometimes, the residual lifetimes can be different among subjects with different covariates or backgrounds. For example, the HIV patients with different ages may have different residual lifetimes, indicating that the quantile residual lifetime depends on some covariates. And the patients are more interested in the quantile residual lifetime of the patients like one's, for instance, patients of the same age. To take into account the effects of covariates, Jung, Jeong and Bandos (2009) proposed a linear regression model for quantile residual lifetime, while Ma and Wei (2012) considered a time-varying coefficient quantile residual life model and estimated the varying coefficients via spline approximation. Recently, Lin, Zhang and Zhou (2015) studied the conditional quantile residual lifetime under different covariates effects by means of an auxiliary model which is specified for the conditional survival function. But this method is not universal for all cases because different auxiliary models need diversified estimation methods.

In this paper, we develop a nonparametric inference on quantile residual lifetime which incorporates covariates but leave the form of the covariates unspecified. This can be achieved by employing the local Kaplan-Meier estimator (Gonzalez-Manteiga and Cadarso-Suarez 1994) and its consistency and asymptotic normality guarantee the asymptotic properties of the proposed estimate of the conditional quantile residual lifetime. The adoption of local Kaplan-Meier estimator makes the method have a flexible applicability, but it also brings challenge to estimate the asymptotic variance of the estimator. In this paper, we adopt the resampling method for nonsmooth estimating functions proposed by Zeng and Lin (2008) to settle this problem.

The rest of the paper is organized as follows. In Section 2, we introduce the conditional quantile residual lifetime model and present the estimation procedure. In Section 3, we derive the asymptotic properties of the proposed estimator and propose the resamping method to estimate the variance. In Section 4, we conduct simulation studies to examine the finite sample properties of the proposed estimators and we also illustrate the proposed methods with a real data example. And we give some concluding remarks in Section 5. All proofs of results are postponed in Appendix.

2. CONDITIONAL QUANTILE RESIDUAL LIFETIME AND INFERENCE PROCEDURES

Let T_i and C_i be the failure time and potential censoring time for subject i, respectively, and $X_i = \min(T_i, C_i)$ be the observed survival time. Let $\delta_i = I(T_i \le C_i)$ be the censoring indicator, where $I(\cdot)$ is the indictor function. Suppose that the failure time T_i depends on a p-dimensional covariate $\mathbf{Z}_i = (Z_{i1}, \cdots, Z_{ip})^T$ and assume that C_i is independent of T_i given covariates $\mathbf{Z}_i$. In addition, the observations $(X_i, \delta_i, \mathbf{Z}_i)$ are assumed to be independent and identically distributed for $i = 1, \cdots, n$. Let $F(t|\mathbf{z})$ and $G(t|\mathbf{z})$ be the distribution functions of T_i and C_i, respectively, given covariate $\mathbf{Z} = \mathbf{z}$. And $S(t|\mathbf{z}) = 1 - F(t|\mathbf{z})$ is the conditional survival distribution. Then $X_i (i = 1, 2, \cdots, n)$ are i.i.d. random variables given $\mathbf{Z}_i$ with distribution function $H(t|\mathbf{z})$ satisfying $1 - H(t|\mathbf{z}) = (1 - F(t|\mathbf{z}))(1 - G(t|\mathbf{z}))$. For any distribution function L, denote $\tau_L = arg \max_t L(t)$. Hence $\tau_H = \tau_F \wedge \tau_G$, in which $a \wedge b$ denotes $\min(a, b)$. We assume that $\tau \le \tau_H$ is the largest follow-up time of the study.

Our goal is to infer the conditional quantile residual lifetime at a time point t_0 given covariate $\mathbf{z}$, which is defined as

$$(1) \quad \theta_\alpha(t_0|\mathbf{z}) = \alpha\text{-quantile}(T - t_0 | T \ge t_0, \mathbf{Z} = \mathbf{z}).$$

Often, the covariate is modeled through a particular form, but we don't specify it here. Definition (1) means that the αth quantile of remaining lifetime among survivors beyond time t_0 given covariate $\mathbf{z}$ equals to $\theta_\alpha(t_0|\mathbf{z})$. This can be equivalently expressed as

$$P\{T - t_0 \ge \theta_\alpha(t_0|\mathbf{z}) | T \ge t_0, \mathbf{z}\} = 1 - \alpha,$$

which implies that

$$P\{T - t_0 \ge \theta_\alpha(t_0|\mathbf{z}) | \mathbf{z}\} = (1 - \alpha) P(T \ge t_0 | \mathbf{z}).$$

Given a time point t_0 and covariate $\mathbf{z}$, let $\theta_{\alpha 0}(t_0|\mathbf{z})$ be the solution of the following equation

$$(2) \; U(\theta_\alpha(t_0|\mathbf{z})) = S(t_0 + \theta_\alpha(t_0|\mathbf{z})|\mathbf{z}) - (1 - \alpha) S(t_0|\mathbf{z}) = 0.$$

And the conditional quantile residual lifetime can be estimated by solving the following estimating equation

$$(3) \; \hat{U}(\theta_\alpha(t_0|\mathbf{z})) = \hat{S}(t_0 + \theta_\alpha(t_0|\mathbf{z})|\mathbf{z}) - (1 - \alpha) \hat{S}(t_0|\mathbf{z}) = 0,$$

where $\hat{S}(t|\mathbf{z})$ is a consistent estimate of the conditional survival distribution function $S(t|\mathbf{z})$. Note that there may exist several solutions to (2), and the definition of the solution can be modified by $\theta_{\alpha 0}(t_0|\mathbf{z}) = \inf\{\theta_\alpha(t_0|\mathbf{z}) : S(t_0 + \theta_\alpha(t_0|\mathbf{z})|\mathbf{z}) \le (1 - \alpha) S(t_0|\mathbf{z})\}$, which is equivalent to

$\theta_{\alpha 0}(t_0|\mathbf{z}) = S^{-1}((1-\alpha)S(t_0|\mathbf{z})|\mathbf{z}) - t_0$, where $S^{-1}(\theta_\alpha|\mathbf{z}) = \inf\{t : S(t|\mathbf{z}) \le 1-\alpha\}$. Similarly, we can define the unique solution to (3) as $\hat{\theta}_\alpha(t_0|\mathbf{z}) = \hat{S}^{-1}((1-\alpha)\hat{S}(t_0|\mathbf{z})|\mathbf{z}) - t_0$.

In this paper, we use the local Kaplan-Meier estimator (Gonzalez-Manteiga and Cadarso-Suarez 1994) to replace $S(\cdot|\mathbf{z})$ and it is defined as

$$\hat{S}(t|\mathbf{z}) = \prod_{i=1}^{n} \left\{ 1 - \frac{B_i(\mathbf{z})}{\sum_{j=1}^{n} B_j(\mathbf{z}) I(X_j \ge X_i)} \right\}^{I(X_i \le t, \delta_i = 1)}$$

if $t < X_{(n)}$ and $\hat{S}(t|\mathbf{z}) = 0$ otherwise, where the weights $B_i(\mathbf{z})$ $(i = 1, 2 \cdots, n)$ are nonnegative and add up to 1, and $X_{(n)} = \max_{1 \le i \le n} X_i$. When $B_i(\mathbf{z}) = 1/n$ for all i, $\hat{S}(t|\mathbf{z})$ reduces to the classical Kaplan-Meier estimator (Kaplan and Meier 1985). There are two types of weights discussed in the literature, Gasser-Müller type of weights (Van Keilegom and Veraverbeke 1996) and Nadaraya-Watson type weights (Dabrowska 1989). Here, we adopt the second type of weights, defined by the following form when $\mathbf{z}$ is continuous

$$B_i(\mathbf{z}) = \left[\sum_{j=1}^{n} K\left(\frac{\mathbf{z} - \mathbf{Z}_j}{h_n} \right) \right]^{-1} K\left(\frac{\mathbf{z} - \mathbf{Z}_i}{h_n} \right), \ \ i = 1, \cdots, n,$$

where $K(\cdot)$ is a kernel function and h_n is the bandwidth converging to zero as n goes to infinity. The choice of kernel function for nonparametric estimates is not crucial to the performance of the nonparametric estimator and we use the product kernel for the multidimensional covariates. For example, when $p = 2$, we can use kernel $K(z_1, z_2) = K_1(z_1)K_2(z_2)$, where both $K_1(\cdot)$ and $K_2(\cdot)$ are univariate kernel functions with higher orders. In this paper, we adopt the kernel $K(z) = (15/32)(3 - 10z^2 + 7z^4)I(|z| \le 1)$ for each covariate when $p = 2$, which is also used by Leng and Tong (2014).

Remark 1. *In this study, although we focused on continuous covariates, an extension to discrete covaraites is possible by taking the kernel function as an indictor function and the weights can be defined as*

$$B_i(\mathbf{z}) = \left[\sum_{j=1}^{n} I(\mathbf{Z}_j = \mathbf{z}) \right]^{-1} I(\mathbf{Z}_i = \mathbf{z}), \quad i = 1, \cdots, n.$$

For the case of mixture covariates, for example, $\mathbf{Z} = (\mathbf{V}^T, \mathbf{W}^T)^T$, *where* $\mathbf{V}$ *is a continuous vector and* $\mathbf{W}$ *is a discrete vector. Then weights* $B_i(\mathbf{z})$ *can be modified as*

$$\widetilde{B}_i(\mathbf{z}) = \left[\sum_{j=1}^{n} \phi(\mathbf{z}_j) \right]^{-1} \phi(\mathbf{z}_i), \quad i = 1, \cdots, n,$$

where $\phi(\mathbf{z}_i) = K\left(\frac{\mathbf{v} - \mathbf{V}_i}{h_n} \right) I(\mathbf{W}_i = \mathbf{w})$. *Furthermore, for the discrete and mixture covariates cases, the asymptotic properties of estimators should be made corresponding adjustments.*

3. ASYMPTOTIC PROPERTIES AND RESAMPLING PROCEDURE

According to the definition of $\hat{\theta}_\alpha(t_0|\mathbf{z})$, we can prove that it is consistent and asymptotically normal. Let $f_{\mathbf{Z}}(\mathbf{z})$ be the marginal density function of $\mathbf{Z}$. Here, we will treat $\mathbf{z}$ as univariate and discuss the multidimensional case in Appendix. To derive the asymptotic properties, we need the following regularity conditions.

(C1) T and C are conditionally independent given the covariate Z.

(C2) The functions $F(\cdot|z)$ and $G(\cdot|z)$ have first-order derivatives with respect to t, denoted as $f(t|z)$ and $g(t|z)$, which are uniformly bounded away from infinity and have bounded (uniformly in t) first-order derivatives with respect to z.

(C3) The first-order derivative of kernel function $K(\cdot)$ is Lipschitz-continuous with compact support and $K(\cdot)$ satisfies $\int K(u)du = 1$, $\int uK(u)du = 0$, $\int K^2(u)du < \infty$ and $\int u^2 K(u)du < \infty$.

(C4) The bandwidth h_n satisfies $h_n = O(n^{-v})$, where $1/4 < v < 1/2$.

The following theorems state the consistency and asymptotic normality of $\hat{\theta}_\alpha(t_0|z)$, respectively.

Theorem 1. *Under conditions (C1)–(C4),* $\hat{\theta}_\alpha(t_0|z)$ *converges to* $\theta_{\alpha 0}(t_0|z)$ *in probability for any* $0 < t_0 < \tau$.

Theorem 2. *Under conditions (C1)–(C4) and* $1/4 < v < 1/3$, *we have* $\sqrt{nh_n}\{\hat{\theta}_\alpha(t_0|z) - \theta_{\alpha 0}(t_0|z)\}$ *converges to a normal distribution with mean 0 and covariance* σ^2 *for a given time point* t_0 *and covariate* z, *where*

$$\sigma^2 = \frac{(1-\alpha)^2 S^2(t_0|z)}{f^2(t_0 + \theta_{\alpha 0}(t_0|z)|z)} f_z(z) \nu^2 \varphi(t_0, \theta_{\alpha 0}(t_0|z)),$$

$$\varphi(t_0, \theta_{\alpha 0}(t_0|z)) = \int_{t_0}^{t_0 + \theta_{\alpha 0}(t_0|z)} \frac{-dS(u|z)}{S^2(u|z)(1 - G(u|z))}$$

and $\nu^2 = \int K^2(u)du$.

It is natural to estimate the variance directly by plug-in method, that is, replacing all the unknown quantities in σ^2 with the corresponding estimated ones. However, σ^2 has a complicated expression involving both density functions and distribution functions. From Appendix, we note that, uniformly in a neighborhood of $\theta_{\alpha 0}(t_0|z)$,

$$\begin{aligned} & \sqrt{nh_n}\hat{U}(\theta_\alpha(t_0|z)) \\ = \ & \frac{1}{\sqrt{nh_n}} \sum_{i=1}^{n} S_i + A\sqrt{nh_n}\{\theta_\alpha(t_0|z) - \theta_{\alpha 0}(t_0|z)\} + o_p(1), \end{aligned}$$

where

Table 1. Simulation results for Cox model

CR	α	$\theta_{\alpha 0}$	Local Kaplan-Meier				Cox model			
			Bias	SE	SD	CP	Bias	SE	SD	CP
20%	0.1	0.6634	-0.0050	0.0737	0.0763	94.4	0.0049	0.0576	0.0590	95.2
	0.3	1.2961	-0.0104	0.0855	0.0857	94.0	0.0077	0.0658	0.0663	93.8
$t_0 = 0.1$	0.5	1.8438	-0.0094	0.1011	0.0978	93.2	0.0051	0.0773	0.0748	94.6
	0.7	2.4604	0.0087	0.1260	0.1181	94.4	0.0029	0.0928	0.0903	95.3
	0.9	3.4395	0.0768	0.1877	0.1776	94.2	0.0021	0.1355	0.1352	93.4
40%	0.1	0.6634	-0.0063	0.0702	0.0805	96.5	0.0037	0.0557	0.0628	94.0
	0.3	1.2961	-0.0083	0.0935	0.0928	93.4	0.0099	0.0706	0.0725	94.1
$t_0 = 0.1$	0.5	1.8438	-0.0029	0.1107	0.1095	94.8	0.0104	0.0866	0.0850	93.9
	0.7	2.4604	0.0220	0.1449	0.1370	93.7	0.0075	0.1094	0.1035	93.5
	0.9	3.4395	0.0838	0.2245	0.2338	92.6	0.0148	0.2067	0.2180	93.9
20%	0.1	0.4071	-0.0040	0.0587	0.0672	95.0	0.0018	0.0442	0.0521	94.6
	0.3	0.9796	-0.0081	0.0881	0.0836	93.3	0.0054	0.0669	0.0652	93.9
$t_0 = 0.5$	0.5	1.5046	-0.0050	0.1007	0.0982	93.8	0.0047	0.0776	0.0748	93.9
	0.7	2.1068	0.0155	0.1210	0.1196	94.2	0.0048	0.0905	0.0893	93.4
	0.9	3.0733	0.0861	0.1870	0.1855	94.8	-0.0005	0.1390	0.1466	95.2
40%	0.1	0.4071	-0.0051	0.0568	0.0708	96.0	0.0015	0.0423	0.0562	95.8
	0.3	0.9796	-0.0095	0.0907	0.0909	93.9	0.0053	0.0700	0.0697	94.4
$t_0 = 0.5$	0.5	1.5046	-0.0017	0.1146	0.1094	93.8	0.0046	0.0871	0.0842	93.1
	0.7	2.1068	0.0192	0.1449	0.1400	94.7	0.0106	0.1114	0.2034	94.4
	0.9	3.0733	0.0817	0.2233	0.2380	94.1	0.0154	0.2190	0.2255	93.7

Note: CR is the censoring ratios; Bias, SE and SD are the bias, standard error and standard deviation of the parameter estimator; CP is the coverage probability of the 95% confidence interval.

$$S_i = -(1-\alpha)S(t_0|z)K\left(\frac{z-Z_i}{h_n}\right) \times \left[\int_{t_0}^{t_0+\theta_{\alpha 0}(t_0|z)} \frac{I(u \le X_i)dS(u|z)}{S^2(u|z)(1-G(u|z))} + \frac{I(t_0 < X_i \le t_0+\theta_{\alpha 0}(t_0|z), \delta_i = 1)}{S(X_i|z)(1-G(X_i|z))}\right],$$

and $A = -f(t_0 + \theta_{\alpha 0}(t_0|z)|z)$. Note that $\sigma^2 = A^{-2}V$, where $V = \lim_{n\to\infty} \frac{1}{nh_n}\sum_{i=1}^n S_i^2$. Thus we can adopt the resampling method proposed by Zeng and Lin (2008) to estimate A. Meanwhile, to avoid estimating S_i directly, we use the bootstrap sample. We sketch the modified resampling procedure as follows.

Step 1 Generate B realizations of ζ which is a zero-mean random variable independent of the data, denoted by $\zeta_1, \cdots, \zeta_B$. Let $\mathbf{x} = (\zeta_1, \cdots, \zeta_B)^T$.

Step 2 Calculate $y_b = \sqrt{nh_n}\hat{U}(\hat{\theta}_\alpha(t_0|z) + \sqrt{nh_n}\zeta_b)$ for $b = 1, \cdots, B$ and denote $Y = (y_1, \cdots, y_B)^T$, then the estimate of A is $\hat{A} = (\mathbf{x}^T\mathbf{x})^{-1}\mathbf{x}^T Y$.

Step 3 The variance σ^2 can be estimated by $\hat{A}^{-2}\hat{V}$ and $\hat{V}$ is the sample variance of $\sqrt{nh_n}U^*(\hat{\theta}_\alpha(t_0|z))$. Here, we draw with replacement $\{X_i^*, \delta_i^*, Z_i^*\}_{i=1}^n$ from the original data set $\{(X_i, \delta_i, Z_i)\}_{i=1}^n$ and calculate the estimating equations $\sqrt{nh_n}\hat{U}(\hat{\theta}_\alpha(t_0|z))$ as $\sqrt{nh_n}U^*(\hat{\theta}_\alpha(t_0|z))$. This process is repeated B times and the sample variance of $\sqrt{nh_n}U^*(\hat{\theta}_\alpha(t_0|z))$ can be used to approximate V.

4. NUMERICAL STUDIES

4.1 Simulations

In this section, we conduct simulation studies to assess the finite sample properties of the proposed estimator and the effectiveness of the resampling procedure. We also make a comparison between the proposed method and the method based on auxiliary model (Lin, Zhang and Zhou, 2015).

Lin, Zhang and Zhou (2015) specified a Cox proportional hazards model for the survival time. Thus in this simulation, we generate the failure times from the following Cox model

$$\lambda(t|Z_1, Z_2) = \lambda_0(t)\exp\{\beta_1 Z_1 + \beta_2 Z_2\},$$

where $\lambda_0(t) = t$ and $\beta_1 = -0.5$, $\beta_2 = 1$. The covariates Z_1 and Z_2 are generated from normal distribution $N(1, 0.5^2)$ and uniform distribution between -1 and 0, respectively. The censoring time follows the exponential distribution with mean c_0, which is set to be 9.4 and 3.8 and the corresponding censoring ratios are 20% and 40%, respectively. We use both the proposed method and the method based on Cox model (Lin, Zhang and Zhou, 2015) to estimate different quantiles of the residual lifetime at different time points $t_0 = 0.1$ and $t_0 = 0.5$ given the covariates $\mathbf{z}_0 = [1, -0.5]^T$. In all simulations, we conduct 1,000 replicates with sample size $n = 400$ and resampling times $B = 500$. The bandwidth of the local Kaplan-Meier estimator is $h_1 = h_2 = n^{-1/6+0.01}$. The results are presented in Table 1. From Table 1, we can see that both of the methods are consistent and the resampling method performs well because SEs and SDs are very close

Table 2. Simulation results for additive hazards model

CR	α	$\theta_{\alpha 0}$	Local Kaplan-Meier Bias	SE	SD	CP	Cox model Bias	SE	SD	CP
20%	0.1	0.1160	0.0003	0.0163	0.0267	95.9	0.0023	0.0128	0.0188	97.9
	0.3	0.3483	0.0017	0.0365	0.0391	95.2	0.0092	0.0288	0.0303	94.5
$t_0 = 0.1$	0.5	0.6022	0.0053	0.0494	0.0503	95.8	0.0152	0.0399	0.0392	93.1
	0.7	0.9193	0.0088	0.0647	0.0646	94.6	0.0150	0.0505	0.0501	92.7
	0.9	1.4582	0.0099	0.1042	0.1016	93.3	0.0128	0.0790	0.0800	93.9
40%	0.1	0.1160	0.0001	0.0170	0.0275	95.1	0.0020	0.0131	0.0195	97.4
	0.3	0.3483	0.0047	0.0393	0.0420	96.9	0.0122	0.0316	0.0325	94.7
$t_0 = 0.1$	0.5	0.6022	0.0079	0.0534	0.0558	95.5	0.0170	0.0415	0.0439	93.8
	0.7	0.9193	0.0099	0.0743	0.0756	95.6	0.0178	0.0566	0.0604	94.5
	0.9	1.4582	0.0031	0.1084	0.1349	93.3	0.0049	0.0870	0.0993	93.9
20%	0.1	0.0816	0.0003	0.0088	0.0225	96.9	0.0003	0.0073	0.0178	96.4
	0.3	0.2586	0.0053	0.0347	0.0401	97.0	0.0067	0.0281	0.0314	95.6
$t_0 = 0.5$	0.5	0.4672	0.0083	0.0505	0.0541	96.3	0.0085	0.0410	0.0419	92.7
	0.7	0.7426	0.0078	0.0693	0.0723	95.4	0.0111	0.0573	0.0566	93.7
	0.9	1.2335	0.0017	0.1041	0.1153	93.5	0.0064	0.0866	0.1135	93.6
40%	0.1	0.0816	-0.0004	0.0085	0.0103	96.7	-0.0004	0.0068	0.0101	96.2
	0.3	0.2586	0.0015	0.0319	0.0360	96.3	0.0039	0.0270	0.0363	96.7
$t_0 = 0.5$	0.5	0.4672	0.0037	0.0569	0.0645	95.2	0.0055	0.0433	0.0512	95.3
	0.7	0.7426	0.0047	0.0756	0.0922	95.0	0.0072	0.0578	0.0773	94.8
	0.9	1.2335	0.0031	0.0850	0.0794	96.7	0.0052	0.0721	0.0827	95.6

for all estimates and the empirical coverage probabilities of the 95% confidence intervals are all around 95%. The estimates based on the Cox model have better properties in terms of smaller biases and SDs(SEs), and this is reasonable since it uses the right model while the local Kaplan-Meier estimator doesn't make use of the information of the model. However, the estimates based on local Kaplan-Meier estimator are also considered acceptable.

In the second simulation, we consider the additive hazards model for the failure time

$$\lambda(t|Z_1, Z_2) = t + \beta_1 Z_1 + \beta_2 Z_2, \tag{4}$$

where $\beta_1 = 0.5$ and $\beta_2 = -0.5$. The covariates Z_1 and Z_2 are generated using the same methods as above. We also generate the censoring variable from exponential distribution with mean 3.2 or 1.3. We use the two methods to estimate the quantiles residual lifetime but we still take model (4) as a Cox model while we apply the method of Lin, Zhang and Zhou (2015). We summarize the results in Table 2. This table shows that the biases of the proposed estimates are much smaller than that of the estimates based on the Cox model because of model misspecification, which means that the proposed method provides more accurate estimates under such circumstances. Thus we propose to use the local Kaplan-Meier estimator if the underlying model is unknown.

In the third simulation, we consider the case with more covariates. The failure times are generated from the following Cox model

$$\lambda(t|Z_1, Z_2) = \lambda_0(t) \exp\{\beta_1 Z_1 + \beta_2 Z_2 + \beta_3 Z_3\},$$

where $\lambda_0(t) = t$ and $\beta_1 = -1$, $\beta_2 = 1.5$, $\beta_3 = -0.5$. The covariates Z_1 and Z_2 are generated from normal distribution $N(1, 0.5^2)$ and uniform distribution between 0 and 1, respectively. And the covariate Z_3 is generated from exponential distribution with mean 0.5. The censoring variable is also generated form the exponential distribution with mean 7.5 and 3, and the corresponding censoring ratios are 20% and 40%, respectively. We use the proposed method to estimate different quantiles of the residual lifetime at the time point $t_0 = 0.5$ given the covariates $\mathbf{z}_0 = [1, 0.5, 0.5]^T$. And the true values of $\theta_\alpha(t_0|z_0)$ for $\alpha = 0.1, 0.3, 0.5, 0.7, 0.9$ are $0.2729, 0.6942, 1.0924, 1.5543, 2.3005$, respectively. In this simulation, the sample size is $n = 400$. The bandwidth is $h_1 = h_2 = h_3 = n^{-1/9+0.01}$ for the local Kaplan-Meier estimator. And we plot the empirical distribution for the estimates of quantile residual lifetime based on 1,000 replications in Figure 1. From this figure, we can see that the empirical distribution of the estimates is normal distribution and the estimates are all unbiased because the mean of the normal distribution and the true value of $\theta_\alpha(t_0|z_0)$ are very close. This indicates that the proposed method performs well for the case with more covariates.

4.2 Real data analysis

We illustrate the proposed method by analyzing HIV data (Hosmer and Lemeshow, 1998). This dataset collected information of 100 HIV positive subjects using a follow-up study. The subjects were enrolled in the study at different time from January 1, 1989 to December 31, 1991 and they were followed until death from AIDS or AIDS-related complications, until the subject was lost to follow-up or to the end

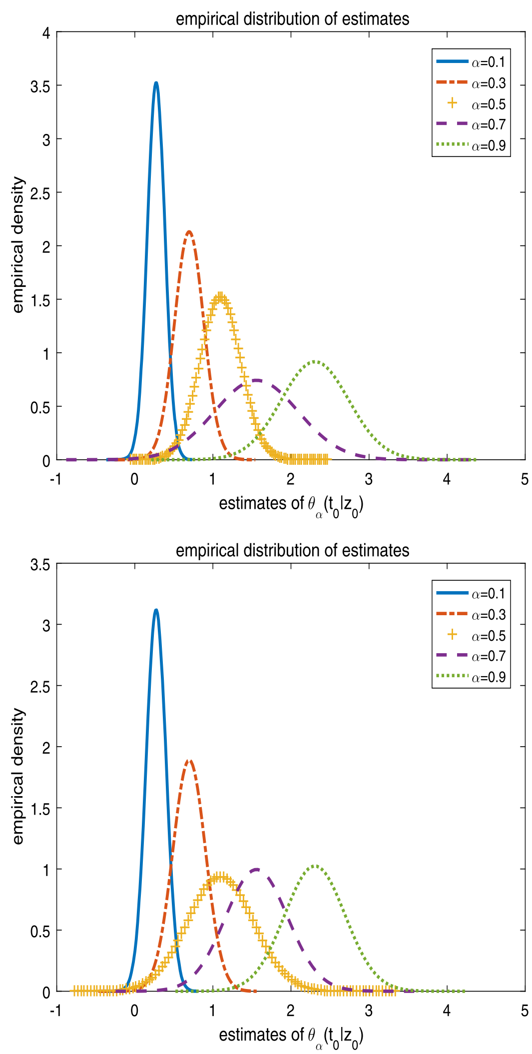

Figure 1. Empirical distribution of the estimates, the censoring ratios of the two figures are 20% and 40%, respectively.

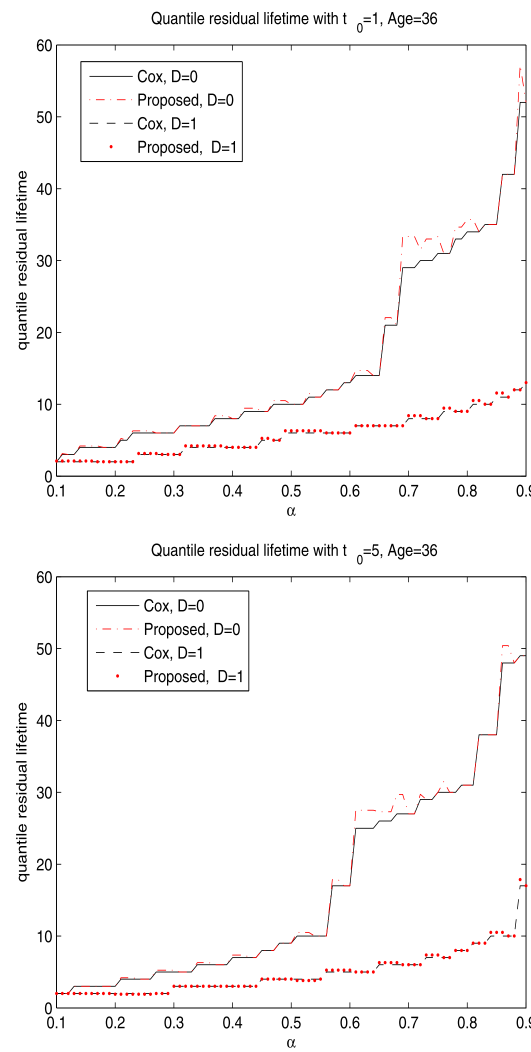

Figure 2. Quantile residual lifetime for HIV data.

of the study on December 31, 1995. Information recorded for the subjects included the follow-up time (the number of months between the entry date and the end date) and covariates such as Age (in years) and Drug indicating prior drug use (D=1=Yes, D=0=No). There were 20 subjects censored and the censoring indicators were also recorded. In this study, we are interested in the trend of the quantile residual lifetime over quantile and time. We use the proposed method and Cox model-based method to estimate $\theta_\alpha(t|\mathbf{z}_0)$. To apply the proposed method, we use the Gaussian kernel for the covariate Age and the bandwidth $h = n^{-1/3+0.01}$ for the local Kaplan-Meier estimator.

First, we plot the curve of quantile residual lifetime function over quantile given time point $t_0 = 1$ or 5 and covariate $Age = 36$ for $D = 0$ or 1 in Figure 2. Here, the sample mode and median of the survival time are 1 and 5, respectively, and the mean of Age is 36. From Figure 2 we can see that the estimates using the two methods almost agree with each other. For a given time point and covariates, the quantile residual lifetime function increases monotonically with increasing quantiles. Another interesting phenomena is that the quantile residual lifetime function curve for no-drug group is above that of drug group given other information, which means that the residual lifetime for the subjects without drug history is longer than that for the patients with drug history, which also coincides with the results of Lin, Zhang and Zhou (2015). Moreover, the difference tends to be more marked among big quantiles. Second, we study the trend of the quantile residual lifetime over time point by plotting the median residual lifetime curve over t given covariates, see Figure 3. From this figure we find that the median residual lifetime is not a monotonic function over time and it indicates that subjects who suffered from AIDS for a short or long time have a relatively shorter residual

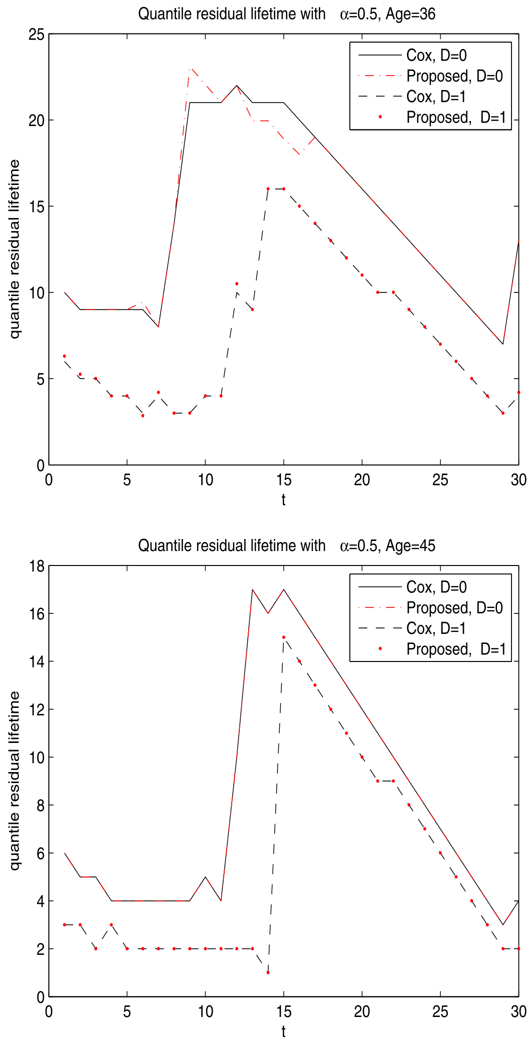

Figure 3. Median residual lifetime for HIV data.

lifetime. Figure 3 also shows that drug experience is adverse to the residual lifetime.

5. DISCUSSION

In studies of time to an event, quantile residual lifetime is often of interest in virtue of its advantages over mean and median residual lifetime. In presence of covariates, the conditional quantile residual lifetime is proposed to describe the effect of covaraites on the quantile residual lifetimes at a given time point. In this study, we propose a nonparametric method to infer the conditional quantile residual lifetime by solving an estimating equation, which involves estimating the conditional survival time. To get rid of the constraint of modeling the survival time, the loacl Kaplan-Meier estimator is employed and leads to a wider application. We also establish the asymptotic properties including both consistency and asymptotic normality of the proposed estimator. However, the asymptotic variance involves the value of density of covariates, which is computationally demanding, and we adopt resampling method proposed by Zeng and Lin (2008) to estimate it. At last, we conduct some simulations to assess the finite-sample performance of the estimator and apply the proposed method to HIV survival data. For future research, it is interesting to generalize the corresponding problems with discrete or mixture covariates. In addition, as we did not consider the case with high dimensional covariates, it deserves further study to develop appropriate dimension reduction methods for the conditional survival function before estimating quantile residual lifetime. Besides, we focus on the case of right-censored data, but lifetime data sometimes are length-biased or left-truncated besides right-censored. So it is also worth for further investigation to apply this approach to the case with more complex data structure.

APPENDIX

In this section, we prove the main results in section 3. First, we present a lemma for the local Kaplan-Meier estimator which is also presented in Gonzalez-Manteiga and Cadarso-Suarez (1994).

Lemma 1. *If conditions (C2)–(C4) hold and $p = 1$, then we have*

$$\begin{aligned} &\sup_t \sup_z |\hat{S}(t|z) - S(t|z)| \\ = \ & O_p\{(\log n)^{1/2} n^{-1/2+v/2} + n^{-2v}\}, \\ &\hat{S}(t|z) - S(t|z) \\ = \ & \frac{1}{nh_n} \sum_{i=1}^{n} K\left(\frac{z - Z_i}{h_n}\right) \xi(X_i, \delta_i, t, z) \\ &+ O_p\left\{\left(\frac{\log n}{nh_n}\right)^{3/4} + h_n^2\right\}, \end{aligned} \tag{A.1}$$

where for $i = 1, 2, \cdots, n$,

$$\begin{aligned} \xi(X_i, \delta_i, t, z) \ = \ & -S(t|z)\left[\int_0^{X_i \wedge t} \frac{dS(u|z)}{S^2(u|z)(1 - G(u|z))} \right. \\ & \left. + \frac{I(X_i \le t, \delta_i = 1)}{S(X_i|z)(1 - G(X_i|z))}\right], \end{aligned}$$

for $t < \tau(z)$ with $\inf_z(1 - H(\tau(z)|z)) > 0$.

Proof of Theorem 1. Lemma 1 shows that $\sup_t |\hat{S}(t|z) - S(t|z)| \xrightarrow{\mathcal{P}} 0$ for any given covariate z, and it yields that $\sup_{\theta_\alpha(t_0|z)} |\hat{U}(\theta_\alpha(t_0|z)) - U(\theta_\alpha(t_0|z))| \xrightarrow{\mathcal{P}} 0$. For a given time point and covariate z, there is an unique solution $\theta_{\alpha 0}(t_0|z)$ such that $U(\theta_\alpha(t_0|z)) = 0$. Thus $\hat{\theta}_\alpha(t_0|z)$ is the unique solution of $\hat{U}(\hat{\theta}_\alpha(t_0|z) = 0$ as $n \to \infty$. If there exists $\delta > 0$ such that $|\hat{\theta}_\alpha(t_0|z) - \theta_{\alpha 0}(t_0|z)| > \delta$, we have $|U(\hat{\theta}_\alpha(t_0|z))| > c_0 > 0$ for a constant c_0. But $|\hat{U}(\hat{\theta}_\alpha(t_0|z)) - U(\hat{\theta}_\alpha(t_0|z))| = o_p(1)$, thus $|\hat{U}(\hat{\theta}_\alpha(t_0|z))| > c_0$, which is contradictory with the definition of estimate. Thus $\hat{\theta}_\alpha(t_0|z)$ is consistent. □

Proof of Theorem 2. First, we show that

$$\sup_{|\theta_\alpha(t_0|z)-\theta_{\alpha 0}(t_0|z)|\le\epsilon} |\hat{U}(\theta_\alpha(t_0|z)) - U(\theta_\alpha(t_0|z)) - \hat{U}(\theta_{\alpha 0}(t_0|z)) + U(\theta_{\alpha 0}(t|z))| = o_p(1/\sqrt{nh_n}). \tag{A.2}$$

To simplify the notations, we use θ and θ_0 to denote the parameter and true parameter, respectively. The estimate is consistent and we just need to focus on θ in $\Theta_\epsilon = \{\theta : |\theta - \theta_0| \le \epsilon\}$. According to the definition of estimating equation (2) and (3), we get that $|\hat{U}(\theta) - U(\theta) - \hat{U}(\theta_0) + U(\theta_0)| = |\hat{S}(t_0+\theta|z) - S(t_0+\theta|z) - \hat{S}(t_0+\theta_0|z) + S(t_0+\theta_0|z)|$. By (A.1) and some calculation, we have the following expression

$$\begin{aligned}
&\hat{S}(t_0+\theta|z) - S(t_0+\theta|z) - \hat{S}(t_0+\theta_0|z) + S(t_0+\theta_0|z)\\
=\;& S(t_0+\theta_0|z)\frac{1}{nh_n}\sum_{i=1}^n K\left(\frac{z-Z_i}{h_n}\right)\\
&\times[\eta(X_i,\delta_i,t_0+\theta_0,z) - \eta(X_i,\delta_i,t_0+\theta,z)]\\
&+\{S(t_0+\theta_0|z) - S(t_0+\theta|z)\}\frac{1}{nh_n}\\
&\times\sum_{i=1}^n K\left(\frac{z-Z_i}{h_n}\right)\eta(X_i,\delta_i,t_0+\theta,z)\\
&+O_p\left\{\left(\frac{\log n}{nh_n}\right)^{3/4} + h_n^2\right\}\\
=:\;& I_1 + I_2 + O_p\left\{\left(\frac{\log n}{nh_n}\right)^{3/4} + h_n^2\right\},
\end{aligned}$$

where $\eta(X_i,\delta_i,t,z) = \int_0^{X_i\wedge t}\frac{dS(u|z)}{S^2(u|z)(1-G(u|z))} + \frac{I(X_i\le t,\delta_i=1)}{S(X_i|z)(1-G(X_i|z))}$ and it is easy to show that $E(\eta(X_i,\delta_i,t,z)) = 0$. Thus we have $E(I_1) = 0$. Next, we calculate the variance of I_1. Without loss of generality, we assume that $\theta\le\theta_0$ and denote that $\psi(t_0+\theta, t_0+\theta_0, z, Z_i) = E\left\{\left[\int_{t_0+\theta}^{t_0+\theta_0}\frac{I(u\le X_i)dS(u|z)}{S^2(u|z)(1-G(u|z))} + \frac{I(t_0+\theta<X_i\le t_0+\theta_0,\delta_i=1)}{S(X_i|z)(1-G(X_i|z))}\right]^2\Big|Z_i\right\}$, which is continuous with respect to θ. And it is easy to show that

$$\psi(t_0+\theta, t_0+\theta_0, z, z) = \int_{t_0+\theta}^{t_0+\theta_0}\frac{-dS(u|z)}{S^2(u|z)(1-G(u|z))},$$

which is $o(1)$ when θ is near θ_0. By some calculation, we get that

$$\begin{aligned}
&Var(I_1)\\
=\;& S^2(t_0+\theta_0|z)\frac{1}{nh_n^2}E\left\{K^2\left(\frac{z-Z_i}{h_n}\right)\right.\\
&\left.\times[\eta(X_i,\delta_i,t_0+\theta_0,z) - \eta(X_i,\delta_i,t_0+\theta,z)]^2\right\}\\
=\;& S^2(t_0+\theta_0|z)\frac{1}{nh_n^2}E\left\{K^2\left(\frac{z-Z_i}{h_n}\right)\right.\\
&\left.\times\psi(t_0+\theta, t_0+\theta_0, z, Z_i)\right\}\\
=\;& S^2(t_0+\theta_0|z)\frac{1}{nh_n^2}\int K^2\left(\frac{z-u}{h_n}\right)\\
&\times\psi(t_0+\theta, t_0+\theta_0, z, u)f_z(u)du\\
=\;& \frac{1}{nh_n}S^2(t_0+\theta_0|z)\psi(t_0+\theta, t_0+\theta_0, z, z)f_z(z)\nu^2\\
&+o_p(1)\\
=\;& o_p(1/nh_n),
\end{aligned}$$

for $|\theta-\theta_0|\le\varepsilon$, where $\nu^2 = \int K^2(u)du$. Thus, we get that $I_1 = o_p(1/\sqrt{nh_n})$.

Now, we prove that $I_2 = o_p(1/\sqrt{nh_n})$. As $F(\cdot|z)$ is continuous, we have

$$|S(t_0+\theta_0|z) - S(t_0+\theta|z)| = o(1),$$

for $\theta\in\Theta_\epsilon$. In addition, Corollary 2.1 of Gonzalez-Manteiga and Cadarso-Suarez (1994) yields that

$$\frac{1}{nh_n}\sum_{i=1}^n K\left(\frac{z-Z_i}{h_n}\right)\eta(X_i,\delta_i,t_0+\theta,z) = O_p(1/\sqrt{nh_n}),$$

which means that $I_2 = o_p(1/\sqrt{nh_n})$. Finally, we proved (A.2).

By (A.2) and the fact that $\hat{\theta}_\alpha(t_0|z)$ is consistent, we get that

$$\begin{aligned}
&\sqrt{nh_n}\hat{U}(\hat{\theta}_\alpha(t_0|z))\\
=\;& \sqrt{nh_n}(U(\hat{\theta}_\alpha(t_0|z)) - U(\theta_0)) + \sqrt{nh_n}\hat{U}(\theta_0) + o_p(1)\\
=\;& -f(t_0+\theta_0|z)\sqrt{nh_n}(\hat{\theta}_\alpha(t_0|z) - \theta_0) + \sqrt{nh_n}\hat{U}(\theta_0)\\
&+o_p(1),
\end{aligned}$$

thus

$$\begin{aligned}
&\sqrt{nh_n}(\hat{\theta}_\alpha(t_0|z) - \theta_0)\\
=\;& \frac{1}{f(t_0+\theta_0|z)}\sqrt{nh_n}\hat{U}(\theta_0) + o_p(1),
\end{aligned}$$

where

$$\begin{aligned}
&\sqrt{nh_n}\hat{U}(\theta_0)\\
=\;& \sqrt{nh_n}\{\hat{S}(t_0+\theta_0|z) - S(t_0+\theta_0|z)\}\\
&-(1-\alpha)\sqrt{nh_n}\{\hat{S}(t_0|z) - S(t_0|z)\}\\
=\;& \frac{1}{\sqrt{nh_n}}\sum_{i=1}^n K\left(\frac{z-Z_i}{h_n}\right)[\xi(X_i,\delta_i,t_0+\theta_0,z)\\
&-(1-\alpha)\xi(X_i,\delta_i,t_0,z)] + o_p(1)\\
=\;& -(1-\alpha)S(t_0|z)\frac{1}{\sqrt{nh_n}}\sum_{i=1}^n K\left(\frac{z-Z_i}{h_n}\right)\\
&\times\left[\int_{t_0}^{t_0+\theta_0}\frac{I(u\le X_i)dS(u|z)}{S^2(u|z)(1-G(u|z))}\right.\\
&\left.+\frac{I(t_0<X_i\le t_0+\theta_0,\delta_i=1)}{S(X_i|z)(1-G(X_i|z))}\right] + o_p(1).
\end{aligned}$$

By the central limit theorem, $\sqrt{nh_n}(\hat{\theta}_\alpha(t_0|z)-\theta_0)$ converges to a normal distribution with mean zero and variance σ^2, where

$$\sigma^2 = \frac{(1-\alpha)^2 S^2(t_0|z)}{f^2(t_0+\theta_0|z)}\psi(t_0,t_0+\theta_0,z,z)f_z(z)\nu^2,$$

in which

$$\psi(t_0,t_0+\theta_0,z,z) = \int_{t_0}^{t_0+\theta_0} \frac{-dS(u|z)}{S^2(u|z)(1-G(u|z))}. \qquad \square$$

For the multidimensional covariates, the local Kaplan-Meier estimate $\hat{S}(\cdot|\mathbf{z})$ may have slower convergence rate. Here, we apply the results in Leng and Tong (2014). To prove the consistency of $\hat{\theta}_\alpha(t_0|\mathbf{z})$, we need the uniform consistency of $\hat{S}(\cdot|\mathbf{z})$, and the conditions need to be modified as follows:

(C3') The kernel fucntion K has a bounded compact support and total variation. For $j=1,2,\cdots,p$, K satisfies $\int z_j K(\mathbf{z})d\mathbf{z}=0$

(C4') The bandwidth h_n satisfies $h_n = O(n^{-v})$, where $0 < v < 1/p$.

In the proof of Theorem 2, (A.1) is needed for the univariate case, but it doesn't hold for multidimensional case. If we adopt the higher order kernels, we have the following results:

$$\begin{aligned} &\hat{S}(t|\mathbf{z}) - S(t|\mathbf{z}) \\ = \ &\frac{1}{nh_n^p}\sum_{i=1}^n K\left(\frac{\mathbf{z}-\mathbf{Z}_i}{h_n}\right)\xi(X_i,\delta_i,t,\mathbf{z}) + r_n(t,\mathbf{z}), \end{aligned}$$

where $r_n(t,\mathbf{z}) = O_p\left\{\left(\frac{\log n}{nh_n^p}\right)^{3/4} + h_n^q\right\} = o_p(n^{-1/2})$ if the following conditions replace the original conditions (C2)–(C4).

(C3") The kernel function $K(\cdot)$ is bounded and has order q with bounded compact support in $\mathcal{R}^p$. It satisfies $\int K(\mathbf{z})d\mathbf{z} = 1$, $\int z_1^{u_1}\cdots z_p^{u_p}K(z_1,\cdots,z_p)d\mathbf{z} = 0$ if $0 \neq \sum_{j=1}^p u_j < q$ and $\int z_1^{u_1}\cdots z_p^{u_p}K(z_1,\cdots,z_p)d\mathbf{z} \neq 0$ if $\sum_{j=1}^p u_j = q$.

(C2") The first q partial derivatives with respect to z of the density function $f_{\mathbf{Z}}(\mathbf{z})$ are uniformly bounded for $\mathbf{z} \in \mathcal{Z}$, and $f(t|\mathbf{z})$ and $g(t|\mathbf{z})$ are uniformly bounded away from infinity and have bounded (uniformly in t) first q order partial derivatives with respect to $\mathbf{z}$.

(C4") The bandwidth h_n satisfies $h_n = O(n^{-v})$, where $1/2q < v < 1/3p$.

Theorem 3. *Under conditions (C1), (C2), (C3') and (C4'), Theorem 1 still holds for multidimensional case. And if conditions (C1) and (C2")–(C4") hold,* $\sqrt{nh_n^p}(\hat{\theta}_\alpha(t_0|\mathbf{z}) - \theta_{\alpha 0}(t_0|\mathbf{z}))$ *converges to a normal distribution with mean zero and variance* σ^2.

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