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A Bartlett Type Correction for Rao's Score Test in Cox Regression Model

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Abstract

Gu and Zheng (1993) established a Bartlett adjustment for the partial likelihood ratio test in the Cox proportional hazards regression model. It is known that the same method of adjustment cannot be used to improve the accuracy of the test statistic derived by Rao's score method. In this paper, the method of Cordeiro and Ferrari (1991) is used to derive a Bartlett type correction for the score test in the Cox proportional hazards regression model. As a special case, a test which is more accurate than the popular log-rank test is obtained.

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1 Introduction

Let $y_i = (T_i, C_i, Z_i)$, $i = 1, \cdots, n$ be independent and identically distributed as $y = (T, C, Z)$, where T is a failure time, C is a censoring time, Z is a covariate taking values on a bounded subinterval of R, and T and C are conditionally independent given Z. Suppose further that the conditional distribution of T given Z follows the Cox proportional hazards regression model (Cox, 1972); that is, assume that $P\{T \geq t|Z\} = \exp\{-\Lambda(t|Z)\}$, where $\Lambda(t|Z) = \Lambda_0(t)\exp(\beta Z)$, $\beta \in \mathcal{B} \subset R$ for an open interval $\mathcal{B}$, and $\Lambda_0(t) = \int_0^t \lambda_0(u)du$ for an unspecified positive continuous functions $\lambda_0(\cdot)$.

Let $X_i = \min(T_i, C_i)$, $\delta_i = I(X_i \le C_i)$, $N_i(t) = I(X_i \le t, \delta_i = 1)$, $M_i(t) = N_i(t) - \int_0^t \exp(\beta Z_i) I(X_i \ge s)\lambda_0(s)ds$, and $Y_i(t) = I(X_i \ge t)$. Throughout this paper, we define $\pi(t) = E\{Y_1(t)\} = P\{X_1 \ge t\}$.

Let $S^{(j)}(\beta, t) = n^{-1}\sum_{i=1}^n Z_i^j \exp(\beta Z_i) Y_i(t)$ for $j = 0, 1, 2$. Then, we can define the partial log-likelihood process for β at any time t by

$$l_n(\beta, t) = \sum_{i=1}^n \int_0^t \left[\beta Z_i - \log\{S^{(0)}(\beta, u)\}\right] dN_i(u).$$

The associated score and observed information processes are respectively given by

$$\begin{aligned} U_n(\beta, t) &= \frac{\partial l_n(\beta, t)}{\partial \beta} = \sum_{i=1}^n \int_0^t \left\{Z_i - \frac{S^{(1)}(\beta, u)}{S^{(0)}(\beta, u)}\right\} dN_i(u) \\ &= \sum_{i=1}^n \int_0^t \left\{Z_i - \frac{S^{(1)}(\beta, u)}{S^{(0)}(\beta, u)}\right\} dM_i(u) \end{aligned}$$

and

$$I_n(\beta, t) = \frac{\partial^2 l_n(\beta, t)}{\partial \beta^2} = \sum_{i=1}^n \int_0^t \left[\frac{S^{(2)}(\beta, u)}{S^{(0)}(\beta, u)} - \left\{\frac{S^{(1)}(\beta, u)}{S^{(0)}(\beta, u)}\right\}^2\right] dN_i(u).$$

Let τ be a known constant such that $\pi(\tau) > 0$, define $l_n(\beta) = l_n(\beta, \tau)$, $U_n(\beta) = U_n(\beta, \tau)$ and $I_n(\beta) = I_n(\beta, \tau)$. Then β can be estimated by $\hat{\beta}$ which satisfies $l_n(\hat{\beta}) = \sup_\beta l_n(\beta)$, or, equivalently, $U_n(\hat{\beta}) = 0$.

In statistical practice, it is often interested in testing the following hypotheses:

$$H_0 : \beta = \beta_0 \text{ vs. } H_1 : \beta \ne \beta_0 \text{ for some known } \beta_0.$$

There are three major methods to test the above hypotheses:

(1) Likelihood ratio test: Reject H_0 if $w = 2[l_n(\hat{\beta}) - l_n(\beta_0)] > C_\alpha$, where C_α is the upper α percentile of the chi-square distribution with one degree of freedom;
(2) Wald test: Reject H_0 if $w = (\hat{\beta} - \beta_0)^2 I_n^{-1}(\hat{\beta}) > C_\alpha$;
(3) Rao's Score test: Reject H_0 if $w = I_n^{-1}(\beta_0) U_n^2(\beta_0) > C_\alpha$.

As n increases, the distributions of all these three tests under null hypothesis approach a central chi-square distribution with one degree of freedom

(Fleming and Harrington, 1991). The convergence rates are expected to be in the order of $O(1/n)$ (Gu, 1992 and Strawderman, 1997). Recently, Gu and Zheng (1993) derived a Bartlett adjustment for the likelihood ratio test to improve its convergence rate. Since score test is more popular in practice as it is easy to calculate and the famous log-rank test in survival analysis is a special case of the score test when Z_i takes only two values 0 and 1, it is of interest to know whether a similar adjustment can be developed for the score test.

Unfortunately, Bickel and Ghosh (1990) proved that, in general, the Bartlett adjustment does not improve the convergence rate of the test derived by Rao's score method. Since then, many researchers have investigated whether a method similar to Bartlett adjustment can be derived to improve the convergence rate of the score test. See Tu and Gross (1996) for references. Tu and Gross (1996) derived a Bartlett type adjustment or correction for the subject-years method or one-sample log-rank test in comparing survival data to a standard population by applying the method of Cordeiro and Ferrari (1991). The major objective of this paper is to generalize the results in that paper to derive a Bartlett type adjustment (or correction) for Rao's score test in the Cox regression model so that the convergence rate of the chi-square approximation to its null distribution can be improved.

This paper is arranged as follows: we first introduce some notation in Section 2. The major results of this paper are stated in Section 3. The application of Bartlett correction to two sample log-rank test and a summary of simulation studies assessing the type I error and power of the Bartlett corrected log-rank test when the sample size is small and moderate are presented in Section 4. The Bartlett corrected log-rank test is also applied in Section 4 to analyze the data from a clinical trial on acute myelogenous leukemia. Section 5 gives a detailed proof for Theorem 1 in Section 3. The paper is concluded with some discussions in Section 6.

2 Notation

We introduce some notations before stating the major results of this paper. Most of these notations are the same as that in Gu and Zheng (1993). Define for $k = 0, \ldots, 4$ and $i = 1, 2, 3$:

$$\begin{aligned}
\alpha_k^{(i)}(t) &= E\big[Z^k \exp\{(i+1)\beta_0 Z\} Y_1(t)\big], \\
\theta_k^{(i)}(t) &= \frac{\alpha_k^{(i)}(t)}{\alpha_0(t)} - 2\alpha_{k-1}^{(i)}(t)\frac{\alpha_1(t)}{\alpha_0^2(t)} + \alpha_{k-2}^{(i)}(t)\frac{\alpha_1^2(t)}{\alpha_0^3(t)}.
\end{aligned}$$

The assumptions given earlier ensure that the $\alpha_k^{(i)}(t)$ are bounded functions for $t \in [0, \tau]$. Let $\theta_k(t) = \theta_k^{(0)}(t)$, and $\alpha_k(t) = \alpha_k^{(0)}(t)$. Define also

$$\begin{aligned}
\Lambda_k(t) &= \int_0^t \frac{\alpha_k(s)}{\alpha_0(s)}\lambda_0(s)ds, \Lambda_1^{(2)}(t) = \int_0^t \frac{\alpha_1^2(s)}{\alpha_0^2(s)}\lambda_0(s)ds,\\
\eta_k(t) &= \frac{\alpha_k^{(1)}(t)}{\alpha_0(t)}\Lambda_0(t) - \frac{\alpha_{k-1}^{(1)}(t)}{\alpha_0(t)}\Lambda_1(t), \eta(t) = -\left(\eta_2(t) - \eta_1(t)\frac{\alpha_1(t)}{\alpha_0(t)}\right).
\end{aligned}$$

From these basic notation, we introduce the following quantities which are related to the moments of the score test statistic:

$$\begin{aligned}
\sigma^2 &= \int_0^\tau \theta_2(t)\alpha_0(t)\lambda_0(t)dt,\\
\Delta &= -\int_0^\tau \left\{\theta_3^{(0)}(u) - \theta_2^{(0)}(u)\frac{\alpha_1(u)}{\alpha_0(u)}\right\}\alpha_0(u)\lambda_0(u)du,\\
\eta &= -\int_0^\tau \left[\theta_3^{(1)}(u)\Lambda_0(u) - \theta_2^{(1)}(u)\left\{\int_0^u \frac{\alpha_1(s)}{\alpha_0(s)}\lambda_0(s)ds\right\}\right]\alpha_0(u)\lambda_0(u)du,\\
\xi &= \frac{7\eta^2}{8\sigma^4} - \frac{1}{8\sigma^2}\{8\mu_4 - 2\mu_5 + 4\mu_6 + 2\mu_7 + 8\mu_8 + 3\nu - 3\sigma^4\},\\
\kappa_4 &= \mu_2 - 4\mu_3 - 12\mu_4 - 24\mu_8 - 3\nu - \frac{9\eta^2}{\sigma^2} + 9\eta^2 + \frac{6\Delta\eta}{\sigma^2},
\end{aligned}$$

where

$$\begin{aligned}
\nu &= \int_0^\tau \theta_2^2(u)\alpha_0(u)\lambda_0(u)du,\\
\mu_2 &= -\int_0^\tau\left\{\theta_4(u) - 2\theta_3(u)\frac{\alpha_1(u)}{\alpha_0(u)} + \theta_2(u)\frac{\alpha_1^2(u)}{\alpha_0^2(u)}\right\}\alpha_0(u)\lambda_0(u)du,\\
\mu_3 &= -\int_0^\tau\left\{\eta_4(u) - 3\eta_3(u)\frac{\alpha_1(u)}{\alpha_0(u)} + 3\eta_2(u)\frac{\alpha_1^2(u)}{\alpha_0^2(u)} - \eta_1(u)\frac{\alpha_1^3(u)}{\alpha_0^3(u)}\right\}\alpha_0(u)\lambda_0(u)du,\\
\mu_4 &= \int_0^\tau \theta_2(u)\eta(u)\alpha_0(u)\lambda_0(u)du,\\
\mu_5 &= \int_0^\tau \theta_2^{(1)}(u)\left\{\Lambda_2(u) - \Lambda_1^{(2)}(u)\right\}\alpha_0(u)\lambda_0(u)du,\\
\mu_6 &= \int_0^\tau\left\{\theta_4^{(2)}(u)\Lambda_0^2(u) - 2\theta_3^{(2)}(u)\Lambda_1(u)\lambda_0(u) + \theta_2^{(2)}(u)\Lambda_1^2(u)\right\}\alpha_0(u)\lambda_0(u)du,\\
\mu_7 &= \int_0^\tau\left\{\theta_4^{(1)}(u)\Lambda_0(u) - 2\theta_3^{(1)}(u)\Lambda_1(u)\lambda_0(u) + \theta_2^{(1)}(u)\Lambda_1^{(2)}(u)\right\}\alpha_0(u)\lambda_0(u)du,\\
\mu_8 &= \int_0^\tau \eta^2(u)\alpha_0(u)\lambda_0(u)du.
\end{aligned}$$

3 Major Results

Let W_n be the score test statistics based on the partial likelihood of Cox regression model with censored data, that is,

$$W_n = I_n^{-1}(\beta_0)U_n^2(\beta_0).$$

Define

$$K_n = I_n^{-1/2}(\beta_0)U_n(\beta_0).$$

Then, $W_n = K_n^2$. To obtain a Bartlett type correction for W, we need first to develop an asymptotic expansion for the distribution of K_n under H_0.

THEOREM 1. *Uniformly in* x,

$$P\{K_n \le x|H_0\} = \Phi(x) + \frac{1}{n^{1/2}}\left\{k_{11} + \frac{1}{6}k_{12}(x^2-1)\right\}\phi(x) + \frac{1}{n}\left\{\frac{k_{21}}{2}x + \frac{k_{22}}{24}(3x - x^3) + \frac{k_{23}}{72}(-x^5 + 10x^3 - 15x)\right\}\phi(x) + o(n^{-1}),$$

where

$$k_{11} = \eta/(2\sigma^3), \quad k_{12} = \Delta/\sigma^3, \quad k_{21} = -\eta^2/(4\sigma^6) - 2\xi/\sigma^2,$$
$$k_{22} = -2\Delta\eta/\sigma^6 + \kappa_4/\sigma^4, \quad k_{23} = \Delta^2/\sigma^6.$$

The proof of this theorem will be deferred to Section 5. An immediate consequence of the above theorem is the following corollary.

COROLLARY 1. (1) *For all* $x > 0$,

$$P\{W_n \le x|H_0\} = P\{K_n \le x^{1/2}|H_0\} - P\{K_n \le -x^{1/2}|H_0\} = P\{\chi_1^2 \le x\} + \frac{1}{n}\left\{k_{21}x^{1/2} + \frac{k_{22}}{12}(3x^{1/2} - x^{3/2}) + \frac{k_{23}}{36}(-x^{5/2} + 10x^{3/2} - 15x^{1/2})\right\} \cdot\phi(x^{1/2}) + o(n^{-1}),$$

where χ_1^2 *is a random variable distributed as central chi-square with one degree of freedom.*

(2) *For* $0 < \alpha < 1$,

$$P\{W_n > (z_{\alpha/2})^2|H_0\} = \alpha + C(\alpha)/n + o(n^{-1}),$$

where

$$C(\alpha) = -\left\{k_{21}z_{\alpha/2} + \frac{k_{22}}{12}(3z_{\alpha/2} - z_{\alpha/2}^3) + \frac{k_{23}}{36}(-z_{\alpha/2}^5 + 10z_{\alpha/2}^3 - 15z_{\alpha/2})\right\}\phi(z_{\alpha/2}).$$

Let $\chi_m(x)$ be the density function of a central chi-square random variable with m degrees of freedom and $f_{W_n}(x)$ be the density function of W_n. Then from the asymptotic expansion for the distribution function of W_n as given in (1) of Corollary 1 and the property of the chi-square density function (Cordeiro and Ferrari, 1991), we have that

$$\begin{aligned} f_{W_n}(x) &= \chi_1(x) + \tfrac{1}{24n}\{A_3\chi_7(x) + (A_2 - 3A_3)\chi_5(x) \\ &\quad +(3A_3 - 2A_2 + A_1)\chi_3(x) + (A_2 - A_1 - A_3)\chi_1(x)\} + o(n^{-1}), \end{aligned} \tag{3.1}$$

where $A_1 = -12k_{21}$, $A_2 = 3k_{22}$, $A_3 = 5k_{23}$, and k_{21}, k_{22}, and k_{23} are defined in Theorem 1. It is easy to see that the above asymptotic expansion for the density function of W_n has the same form as that given by (1) in Cordeiro and Ferrari (1991, p.575) with $r = 1$. Thus, an application of formulae (2) and (3) in Cordeiro and Ferrari (1991) yields the following theorem, which can be easily proved by expanding the moment generating function of W_n under H_0 (see also formula (1) of Cox and Reid, 1987).

THEOREM 2. *Define*

$$W_n^* = \frac{W_n}{1 + (c + bW_n + aW_n^2)},$$

where

$$\begin{aligned} a &= k_{23}/(36n) = \Delta^2/(36n\sigma^2), \\ b &= (3k_{22} - 10k_{23})/(36n) = (-6\Delta\eta + 3\kappa_4\sigma^2 - 10\Delta^2)/(36n\sigma^6), \\ c &= (-12k_{21} - 3k_{22} + 5k_{23})/(12n) \\ &= (3\eta^2 + 24\xi\sigma^4 + 6\Delta\eta - 3\kappa_4\sigma^2 + 5\Delta^2)/(12n\sigma^6). \end{aligned}$$

We have

$$P\{W_n^* > (z_{\alpha/2})^2 | H_0\} = \alpha + o(n^{-1}).$$

W_n^* is called the Bartlett type corrected score test statistic. If we define the accuracy of a test as the difference between its actual type I error and the nominal type I error, then, comparing (2) of Corollary 1 with Theorem 2, we can see that Bartlett type corrected test is more accurate than the original score test.

REMARK. If the baseline hazard function $\lambda_0(t)$ is unspecified and distribution function for the censoring variable is unknown, the constants a, b, and c in the Bartlett type corrected score test statistic have to be estimated from the data. Since they are all functions of $\alpha_k^{(i)}$ and $\Lambda_k(t)$, they can be estimated through the empirical estimates of $\alpha_k^{(i)}$ and $\Lambda_k(t)$ as given by Gu (1992). This does not change the order of the approximation.

4 Example and Simulation Studies

In a balanced two arm clinical trial to compare a new treatment with a standard treatment, we can define a covariate z_i for the i-th patient as: $z_i = 1$ if the patient was assigned a new treatment and $z_i = 0$ if the patient is assigned a standard treatment. Since the trial is balanced, we have $P\{z_i = 1\} = P\{z_i = 0\} = 1/2$. The difference between two treatment groups in terms of failure times can be tested using a Cox model with $\beta_0 = 0$. In this case, the score test is reduced to the popular log-rank test in the survival analysis (Cox and Oakes, 1984). By some calculations, we can get in this case (see also, Gu and Zheng (1993)):

$$\sigma^2 = \Sigma_0/4, \quad \Delta = \eta = 0, \quad \nu = \mu_2 = \Sigma_0/16,$$

$$\mu_3 = -\mu_4 = \mu_5 = \mu_7 = \Sigma_1/16, \quad \mu_6 = \mu_8 = \Sigma_2/16,$$

where

$$\Sigma_k = \int_0^\tau \Lambda_0^k(t)\alpha_0(t)\lambda_0(t)dt = \int_0^\tau \Lambda_0^k(t)\pi(t)\lambda_0(t)dt.$$

These imply that

$$\xi = -\left\{3\Sigma_0/16 - 3\Sigma_0^2/16 - \Sigma_1/2 + 3\Sigma_2/4\right\}/(2\Sigma_0)$$

and

$$\kappa_4 = -\Sigma_0/8 + \Sigma_1/2 - 3\Sigma_2/2.$$

From these we can get a Bartlett adjusted log-rank test statistic with

$$a = 0, \quad b = (-\Sigma_0 + 4\Sigma_1 - 12\Sigma_2)/(18n\Sigma_0^2), \quad c = (3\Sigma_0^2 - \Sigma_0 + 12\Sigma_2)/(4n\Sigma_0^3).$$

When $\lambda_0(t)$ is unknown, Σ_k $(k = 0, 1, 2)$ can be estimated by (Strawderman, 1997)

$$\hat{\Sigma}_k = \frac{1}{n}\sum_{i=1}^n \delta_i\{\hat{\Lambda}(X_i)\}^k,$$

where $\hat{\Lambda}(X_i)$ is the Nelson-Aalen estimator for the cumulative hazard function based on the data from two treatment groups pooled together.

Monte-Carlo simulations have been performed to assess the actual type I error and the powers of the log-rank test and its Bartlett type correction for small and moderate sample sizes ($n = 10$, 20, 30 and 40). In these simulations, $\hat{\Lambda}(X_i)$ is obtained from $-\log$ of the Kaplan-Meier survival time estimate based on pooled data. A clinical trial model used in the simulation studies of Strawderman (1997) was adopted in our simulations to generate the survival data. For each sample size, a series of independent patients was first generated and allocated with equal probability into two treatment arms. The true survival time for each patient allocated to the first arm was generated from an exponential distribution with parameter $\lambda_0 = -\log(0.2)/10$ using SAS function RANEXP. The survival time for a patient in the second treatment arm was generated using the same SAS function from an exponential distribution with parameter $\lambda_1 = \lambda_0$ (i.e., $\beta_0 = 0$) or $\lambda_1 = 1.5\lambda_0$ (i.e., $\exp(\beta_0) = 1.5$), depending on whether the type I error or the power was assessed. Each patient was assumed to enter the study uniformly over L years from the start date of the study and to be followed then for a minimal of B years. This is equivalent to assume that the distribution of the censoring time for each patient was uniform on the interval from B to $L + B$. Three different sets of L and B were used in the simulations which represented respectively light, moderate and heavy censorings: (1) $L = 1$ and $B = 9$; (2) $L = 5$ and $B = 5$ and (3) $L = 9$ and $B = 1$. The nominal significance level of each test was assumed to be 0.05. In each simulation, 3,000 independent random samples were generated. The actual type I error and power of each test were estimated from the proportions of the null hypothesis $H_0 : \lambda_1 = \lambda_0$ being rejected among these 3,000 samples. The results of the simulation studies are presented in Table 1.

TABLE 1. SIMULATED TYPE I ERROR AND POWERS OF THE LOG-RANK TEST AND ITS BARTLETT CORRECTION

	Type I error ($\lambda_1 = \lambda_0$)		Power at $\lambda_1 = 1.5\lambda_0$	
	Log-rank	Bartlett Correction	Log-rank	Barlett Correction
		$L = 1$ and $B = 9$		
$n = 10$	0.061	0.059	0.154	0.145
$n = 20$	0.053	0.041	0.211	0.178
$n = 30$	0.053	0.040	0.284	0.233
$n = 40$	0.042	0.036	0.374	0.308
		$L = 5$ and $B = 5$		
$n = 10$	0.059	0.035	0.121	0.074
$n = 20$	0.056	0.037	0.197	0.140
$n = 30$	0.046	0.034	0.275	0.216
$n = 40$	0.052	0.039	0.374	0.308
		$L = 9$ and $B = 1$		
$n = 10$	0.059	0.048	0.115	0.091
$n = 20$	0.057	0.050	0.170	0.149
$n = 30$	0.059	0.055	0.234	0.214
$n = 40$	0.053	0.051	0.283	0.271

From this table, we may find out that the simulated type I error of the Bartlett corrected log-rank test is always smaller than that of the original log-rank test and less than the nominal level 0.05 in most circumstances. When censoring is heavy, the type I error of the original log-rank test is much higher than the nominal level 0.05. In contrast, in this case, the type I error of the Bartlett corrected log-rank test is very close to the nominal level 0.05. The Bartlett correction sometime went too far. In almost all the cases, the Bartlett corrected log-rank test is slightly less powerful than the original log-rank test. These results are consistent with those obtained by Tu and Gross (1996) for the Bartlett corrected one-sample log-rank test (or the subject-years test as it is often called). The replacement of unknown parameters in the corrected test statistic by empirical estimate may have some impact on the performance of the proposed test when the sample size is small.

Finally, we consider the application the proposed test to the data from a clinical trial evaluating the efficacy of maintenance chemotherapy for acute myelogenous leukemia (AML). The times until relapse for 23 patients randomized after remission through treatment by chemotherapy to receive either maintenance chemotherapy (11 patients) or nothing (12 patients) are given in Table 1.1 of Tableman and Kim (2004). The (uncorrected) log-rank test statistic for the difference between two treatments was 3.32, corresponding to a p-value of 0.065. The Bartlett correction factors for these data were respectively $a = 0$, $b = -0.081$, and $c = 0.427$. This led to a Bartlett corrected log-rank test statistic 2.87 and p-value 0.090, which confirmed that the Bartlett corrected log-rank test is more conservative than the (uncorrected) log-rank test.

5 The Proof of Theorem 1

We introduce more notation to prove Theorem 1. Let

$$\begin{aligned}
g(y_i) &= \int_0^\tau \left\{ Z_i - \frac{\alpha_1(u)}{\alpha_0(u)} \right\} dM_i(u), \\
\xi_{i,k}(t) &= Z_i^k \exp(\beta_0 Z_i) I(X_i \geq t), \\
\rho_i(t) &= \xi_{i,2}(t) - \alpha_2(t) - 2\frac{\alpha_1(t)}{\alpha_0(t)}\{\xi_{i,1}(t) - \alpha_1(t)\} + \frac{\alpha_1^2(t)}{\alpha_0^2(t)}\{\xi_{i,0}(t) - \alpha_0(t)\}, \\
h_1(y_i) &= \int_0^\tau \theta_2(t) dM_i(t), h_2(y_i) = \int_0^\tau \rho_i(t)\lambda_0(t)dt, \\
h(y_i) &= h_1(y_i) + h_2(y_i),
\end{aligned}$$

$$\begin{aligned}
\sigma^2 &= E[g(y_1)]^2, \quad \eta = E[g(y_1)h(y_1)], \\
\pi_i(t) &= \frac{1}{\alpha_0(t)}\{\xi_{i,1}(t)-\alpha_1(t)\} - \frac{\alpha_1(t)}{\alpha_0^2(t)}\{\xi_{i,0}(t)-\alpha_0(t)\}, \\
\psi_0(y_i,y_j) &= -\int_0^\tau \pi_i(t)dM_j(t), \\
\psi_0(y_i) &= \psi_0(y_i,y_i), \psi(y_i,y_j) = \psi_0(y_i,y_j)+\psi_0(y_j,y_i), \\
\omega(y_i,y_j) &= \psi(y_i,y_j) - \frac{1}{2\sigma^2}\{g(y_i)h(y_j)+g(y_j)h(y_i)\}, \\
\Delta &= -E\{g^3(y_1)\} - 3E\{g(y_1)g(y_2)\omega(y_1,y_2)\}, \\
B(y_i,y_j,y_k) &= \sum_{\substack{i_1,i_2,i_3\in\{i,j,k\} \\ i_1,i_2,i_3 \text{ are distinct}}} \int_0^\tau \frac{\xi_{i_1,0}(t)-\alpha_0(t)}{\alpha_0(t)}\pi_{i_2}(t)dM_{i_3}(t), \\
D_1(y_i,y_j) &= \int_0^\tau \left[\frac{\rho_i(t)}{\alpha_0(t)} - \theta_2(t)\frac{\xi_{i,0}(t)-\alpha_0(t)}{\alpha_0(t)}\right] dM_j(t), \\
D_2(y_i,y_j) &= \int_0^\tau \left[\frac{\alpha_1^2(t)}{\alpha_0^3(t)}\{\xi_{i,0}(t)-\alpha_0(t)\}\{\xi_{j,0}(t)-\alpha_0(t)\}\right. \\
&\quad -2\frac{\alpha_1(t)}{\alpha_0^2(t)}\{\xi_{i,1}(t)-\alpha_0(t)\}\{\xi_{j,1}(t)-\alpha_0(t)\} \\
&\quad \left.+\frac{1}{\alpha_0(t)}\{\xi_{i,1}(t)-\alpha_1(t)\}\{\xi_{j,1}(t)-\alpha_1(t)\}\right]\lambda_0(t)dt, \\
C(y_i,y_j) &= D_2(y_i,y_j)+D_2(y_j,y_i)-D_1(y_i,y_j)-D_1(y_j,y_i), \\
A_{ijk} &= h(y_i)\psi(y_j,y_k), B_{ijk} = g(y_i)\{C(y_j,y_k) - \frac{3}{2}h(y_j)h(y_k)\}, \\
\varphi(y_i,y_j,y_k) &= B(y_i,y_j,y_k) - \frac{1}{2\sigma^2}\{A_{ijk}+A_{jik}+A_{kij}+B_{ijk}+B_{jik}+B_{kij}\}, \\
\kappa_4 &= E\{g^4(y_1)\} - 3\sigma^4 + 4E\{g(y_1)g(y_2)g(y_3)\varphi(y_1,y_2,y_3)\} \\
&\quad +12E\{g^2(y_1)g(y_2)\omega(y_1,y_2) + g(y_1)g(y_2)\omega(y_1,y_3)\omega(y_2,y_3)\}.
\end{aligned}$$

From Lemma 2.1 and Lemma 2.2 in Gu and Zheng (1993), we have respectively

$$U_n(\beta_0) = \tilde{U}_n(\beta_0) + R_{1n},$$

where the remainder term R_{1n} is such that for any $p \geq 2$, $E(|R_{1n}|^p) = O(n^{-p})$,

$$\tilde{U}_n(\beta_0) = \sum_{i=1}^n g(y_i) + \frac{1}{n}\sum_{i<j}\psi(y_i,y_j) + \frac{1}{n}\sum_{i=1}^n \psi_0(y_i) + \frac{1}{n^2}\sum_{i<j<k} B(y_i,y_j,y_k),$$

and

$$I_n(\beta_0) = \tilde{I}_n(\beta_0) + R_{2n},$$

where the remainder term R_{2n} is such that for any $p \geq 2$, $E(|R_{2n}|^p) = O(n^{-p/2})$,

$$\begin{aligned}\tilde{I}_n(\beta_0) &= n\sigma^2 + \sum_{i=1}^{n} h(y_i) - \frac{1}{n}\sum_{i<j} C(y_i, y_j) + \gamma, \\ \gamma &= -\int_0^\tau \theta_2^{(1)}(t)\lambda_0(t)dt.\end{aligned}$$

Based on these asymptotic expansions and from Theorem A.1 of Strawderman and Wells (1997), we can write k_n as an asymptotic U-statistic:

$$k_n = I_n^{-1/2}(\beta_0)U_n(\beta_0) = \frac{U_n}{\sigma} - \frac{\eta}{2\sigma^3 n^{1/2}} + R_n,$$

where

$$R_n = o_p(n^{-1})$$

and

$$U_n = \sum_{i=1}^{n}\left[\frac{g(y_i)}{n^{1/2}} + \frac{\chi(y_i)}{n^{3/2}}\right] + \sum_{i<j}\frac{\omega(y_i, y_j)}{n^{3/2}} + \sum_{i<j<k}\frac{\varphi(y_i, y_j, y_k)}{n^{5/2}}$$

with

$$\begin{aligned}\chi(y_i) &= \psi_0(y_i) - \frac{\gamma}{2\sigma^2}g(y_i) + \frac{3\eta}{4\sigma^4}h(y_i) - \frac{1}{2\sigma^2}\{g(y_i)h(y_i) - \eta\} \\ &\quad -\frac{1}{2\sigma^2}\left[E\{g(y_j)C(y_i, y_j)|y_i\} - E\{h(y_j)\psi(y_i, y_j)|y_i\}\right].\end{aligned}$$

Strawderman and Wells (1997, Theorem A.2) derived an Edgeworth expansion for the distribution function of an asymptotic U-statistic. Applying this theorem, we can get

$$\begin{aligned}&P\{I_n^{-1/2}(\beta_0)U_n(\beta_0) \leq x|H_0\} \\ &\quad = \Phi(x') - n^{-1/2}\phi(x')P_1(x') - n^{-1}\phi(x')P_2(x') + o(n^{-1}), \qquad (5.1)\end{aligned}$$

where

$$\begin{aligned}x' &= x + \eta/(2\sigma^3 n^{1/2}), \\ P_1(x) &= \frac{-\Delta}{6\sigma^3}(x^2 - 1), \\ P_2(x) &= \xi\frac{x}{\sigma^2} + \frac{\kappa_4}{24\sigma^4}(x^3 - 3x) + \frac{\Delta^2}{72\sigma^6}(x^5 - 10x^3 + 15x), \\ \text{with } \xi &= E\{g(y_1)\chi(y_1)\} + E\{\omega^2(y_1, y_2)/4\}.\end{aligned}$$

Let $\delta = \eta/(2n^{1/2}\sigma^3)$. Note that $\delta = O(n^{-1/2})$. Applying Taylor Expansion to $\Phi(x+\delta)$ gives

$$\Phi(x+\delta) = \Phi(x) + \delta\phi(x) - x\delta^2\phi(x)/2 + O(n^{-3/2}). \tag{5.2}$$

Similarly,

$$\begin{aligned}
&-n^{-1/2}\phi(x+\delta)P_1(x+\delta)\\
&= -n^{-1/2}\phi(x)P_1(x) + \delta n^{-1/2}\frac{\Delta}{6\sigma^3}(-x^3+3x)\phi(x) + O(n^{-3/2})\\
&= n^{-1/2}\left\{\frac{\Delta}{6\sigma^3}(x^2-1)\right\}\phi(x) + n^{-1}\frac{\eta\Delta}{12\sigma^6}(-x^3+3x)\phi(x) + O(n^{-3/2})
\end{aligned} \tag{5.3}$$

and

$$\begin{aligned}
&-n^{-1}\phi(x+\delta)P_2(x+\delta)\\
&\quad = -n^{-1}\phi(x)P_2(x) + O(n^{-3/2})\\
&\quad = n^{-1}\phi(x)\{-a^*x - b^*(x^3-3x) - c^*(x^5-10x^3+15x)\},
\end{aligned} \tag{5.4}$$

where a^*, b^*, and c^* are the coefficients of $P_2(\cdot)$ defined in (5.1). Combining (5.2)-(5.4), we have

$$\begin{aligned}
&P\{K_n \le x|H_0\}\\
&= \Phi(x) + n^{-1/2}\frac{\eta}{2\sigma^3}\phi(x) + n^{-1}\frac{\eta^2}{8\sigma^6}\phi(x)x + n^{-1/2}\phi(x)\frac{\Delta}{6\sigma^3}(x^2-1)\\
&\quad -n^{-1}\phi(x)\frac{\Delta\eta}{12\sigma^6}(x^3-3x)\\
&\quad +n^{-1}\phi(x)\{-a^*x - b^*(x^3-3x) - c^*(x^5-10x^3+15x)\} + o(n^{-1})\\
&= \Phi(x) + n^{-1/2}\phi(x)\left\{\frac{\eta}{2\sigma^3} + \frac{\Delta}{6\sigma^3}(x^2-1)\right\}\\
&\quad +n^{-1}\phi(x)\left[\frac{1}{2}\left\{-\frac{\eta^2}{4\sigma^6} - \frac{\xi}{\sigma^2}\right\}x\right.\\
&\quad \left.+\frac{1}{24}\left\{\frac{-2\Delta\eta}{\sigma^6} + \frac{\kappa_4}{\sigma^4}\right\}(3x-x^3) + \frac{1}{72}\frac{\Delta^2}{\sigma^6}(-x^5+10x^3-15x)\right] + o(n^{-1}).
\end{aligned}$$

What now remains to show is that σ^2, Δ, η, ξ and κ_4 have the expressions as defined in Section 2. This can be achieved by some complicated calculations which utilize some formulas of moments related to the Cox model as given in the end of Gu and Zheng (1993). The details are omitted.

6 Discussion

In this paper, we have derived a Bartlett type correction to the score test in the Cox regression model. As mentioned in the Introduction, there are three major methods that would be used to construct a test in the Cox regression model: likelihood ratio test, Wald test, and Rao's score test. The Bartlett correction to the likelihood ratio test has been derived by Gu and Zheng (1993). It is of interest to develop the same type of correction to the Wald test and compare corrected version of these three tests. There are also other ways to make the higher order corrections to the test statistics with chi-squared limit distribution. Some of these methods can be found in, for example, Chandra and Mukerjee (1991), Taniguchi (1991), and Lai and Wang (1993). Another interesting research topic is to apply these methods to the three tests in the Cox regression model.

The Cox regression model discussed in this paper is a univariate model with only one covariate. Extension of the results in this paper and the papers by Gu (1992) and Gu and Zheng (1993) to the Cox regression model with multiple covariates is also an interesting but unsolved problem. Cordeiro and Colosimo (1997, 1999) have derived the Bartlett type corrections to respectively likelihood ratio and score tests in a multivariate exponential regression model with type I or II censoring.

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