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Testing homogeneity in Weibull error in variables models

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Abstract We discuss properties of the score statistics for testing the null hypothesis of homogeneity in a Weibull mixing model in which the group effect is modelled as a random variable and some of the covariates are measured with error. The statistics proposed are based on the corrected score approach and they require estimation only under the conventional Weibull model with measurement errors and does not require that the distribution of the random effect be specified. The results in this paper extend results in Gimenez, Bolfarine, and Colosimo (Annals of the Institute of Statistical Mathematics, *52*, 698–711, 2000) for the case of independent Weibull models. A simulation study is provided.

Keywords Homogeneity test · Measurement errors · Corrected score · Accelerated failure time model

1 Introduction

Many failure time regression applications involve covariates that are measured with error. For example, daily intake of saturated fat is imprecisely evaluated; in cardiovascular research blood pressure is often subject to considerable hourly and daily variation (Carroll et al 1995), in AIDS studies, CD4 counts are often measured with substantial amount of variability (Tsiatis et al. 1995).

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Clustered failure time data arise in many contexts such as in familial studies, ages at the onset of a disease are recorded for multiple members of the same family; in multicentric clinical trials failure times are observed for multiple patients in each center. It also follows that the observed survival times of siblings or married couples in human studies or litter mates in animal studies are typically correlated. Frequently, this correlation is due to omitted or neglected variables. In such situations there is natural interest in testing whether there is within group correlation (or heterogeneity across groups) for given covariates.

A number of authors have proposed using the so called shared *frailty model* to account for dependence between survival times. In such models, all individuals within a group share a common unobserved random effect, the *frailty*, which acts in a multiplicative way on each individual hazard rate. However, some authors (see Hougaard et al. 1994; Keiding et al. 1997) present case studies which indicate that modeling survival within a group by an *accelerated failure time model* may be preferable in accounting for heterogeneity in survival times. In accelerated failure time models, the logarithm of the event time follows a linear regression on the covariate vector, and the random effect acts on a multiplicative way on the event times. In this model a natural parametric approach is the Weibull regression model, which according to Kimber (1996) has been applied successfully in a variety of disciplines, including reliability and medical studies.

The score test where all variables are measured correctly (no variables measured with error) has been the subject of several papers in the literature. Some basic results can be found in Cox (1983), Liang (1987) and Dean (1992), among others. Extensions to generalized linear models (Hamerle 1990; Commenges et al. 1994; Jacqmin-Gadda, and Commenges, 1995; Lin 1997) and to survival analysis (Gray 1995; Commenges and Andersen, 1995; Kimber 1996) have also been considered. Commenges and Jaqmin-Gadda (1997) generalizes most of the previous results on homogeneity tests including generalized linear models and proportional hazard models. Some authors propose using the Laplace method for approximating integrals (Breslow and Clayton, 1993; Lin 1997) as a way of approximating the integrals involved in the elimination of the random effects. In survival data, under the accelerated failure time assumption, with a random effect, Bolfarine and Valença (2005) propose score type statistics for testing homogeneity hypothesis using the observed information matrix which is asymptotically equivalent to the score statistics based on the Fisher information matrix.

In this paper, we consider score tests for testing homogeneity in accelerated failure time models with a random effect and covariables measured with errors, and specialize the results for the Weibull model. We consider a functional nondifferential (Bolfarine and Arellano-Valle 1998) additive measurement errors model to describe the random mechanism generating the measurement errors. Use is made of the corrected score approach considered in Nakamura (1990) and Gimenez and Bolfarine (1997). Asymptotic properties of the resulting statistic for testing homogeneity are investigate with simulation studies.

The paper is organized as follows. Section 2 presents the additive Weibull measurement error model. In Sect. 3, a Taylor expansion is considered for the marginal likelihood function. Naive tests of homogeneity are considered in Sect. 4. The corrected score test is derived in Sect. 5. Simulation studies are presented in

Sect. 6. The corrected score vector and observed information matrix are presented in the Appendix.

2 Weibull measurement error models with a random effect

Consider a sample divided into k groups and let T_{ij} be the event time corresponding to the individual j in the group i, with $j = 1, \ldots, n_i$, and $i = 1, \ldots, k$. The log-linear Weibull model with a random effect, models $\log T_{ij}$ as

$$\log\ T_{ij} = U_i + \boldsymbol{\beta}_z^T \mathbf{z}_{ij} + \beta_x x_{ij} + \sigma \epsilon_{ij}, \tag{1}$$

where the $\epsilon_{ij}'s$ are independent and identically distributed (i.i.d.) random errors, with standard extreme value density function given by $f(\epsilon) = \exp(\epsilon - e^{\epsilon})$, $\epsilon \in \Re$. We consider $\mathbf{z}_{ij}$ a covariate vector correctly observed and x_{ij} an unobserved variable which is measured with error. We assume an additive functional measurement error model relating the observed (surrogate) w_{ij} and the unobserved x_{ij}, which is expressed as

$$w_{ij} = x_{ij} + \eta_{ij}, \tag{2}$$

with $\eta_{ij}'s$ representing unobserved i.i.d. errors with distribution $N(0, \phi)$, that is, the normal distribution with mean 0 and variance ϕ. The random effect for group i is represented by

$$U_i = \alpha + \theta^{1/2} V_i, \tag{3}$$

where the $V_i's$ are i.i.d. random variables with $E[V_i] = 0$, $E[V_i^3] = o(\theta^{1/2})$, $E[V_i^2] = 1$ and $E[V_i^m] < \infty$, $m > 3$, and otherwise unspecified distribution function F. We assume that U_i, η_{ij} and ϵ_{ij} are all independent $j = 1, \ldots, n_i$ and $i = 1, \ldots, k$. Hence, under the nondifferential functional additive measurement error model structure specified by Eq. (2), x_{ij} are not observed and hence, maximum likelihood methodology (such as asymptotic inference based on Fisher information matrices) can not be implemented. Inference has to be based on the (surrogate) observed w_{ij}, $j = 1, \ldots, n_i, i = 1, \ldots, k$.

3 Marginal likelihood function

Consider that survival times are subject to right censoring and that censoring is random, uninformative and independent of $U_i, i = 1, \ldots, k$. Set $\delta_{ij} = 1$ to indicate a failure time and $\delta_{ij} = 0$ to indicate a censoring time. Let Y_{ij} be the observed log survival time for subject j in group i. Denote by $\lambda = (\gamma^T, \theta)^T$, the vector of parameters, with $\gamma^T = (\alpha, \boldsymbol{\beta}_z^T, \beta_x, \sigma)$. The hypothesis of homogeneity is then $H_0 : \theta = 0$. The likelihood function with respect to the conditional distribution of (Y_{ij}, δ_{ij}) given V_i for the Weibull model is

$$L_{ij}(\lambda | u(v_i), x_{ij}) = (1/\sigma)^{\delta_{ij}} \exp[\delta_{ij} s(x_{ij}, v_i) - \exp(s(x_{ij}, v_i))], \tag{4}$$

where $u(v_i) = \alpha + \theta^{1/2} v_i$ and $s(x_{ij}, v_i) = (y_{ij} - u(v_i) - \boldsymbol{\beta}_z^T \mathbf{z}_{ij} - \beta_x x_{ij})/\sigma$.

Furthermore, for $v_i = 0$, $L_{ij}(\lambda|u(0), x_{ij}) = L_{ij}(\gamma, x_{ij})$ which depends only on γ. Let $\mathbf{Y}_i = (Y_{i1}, Y_{i2}, \ldots, Y_{in_i})^T$ and $\mathbf{Y} = (\mathbf{Y}_1^T, ..., \mathbf{Y}_k^T)^T$, with similar notation for $\mathbf{x}$, $\mathbf{x}_i$, $\mathbf{w}$ and $\mathbf{w}_i$. The marginal log-likelihood corresponding to the observed sample is given by

$$l(\lambda, \mathbf{x}) = \sum_{i=1}^{k} \log \int \prod_{j=1}^{n_i} L_{ij}(\lambda|u(v_i), x_{ij})\mathrm{d}F(v_i). \tag{5}$$

Since the distribution of V_i in Eq. (3) is not specified (except for moments assumptions) we can not compute analytically the integral in Eq. (5). As considered in Bolfarine and Valença (2005), an approximation follows by considering a Taylor expansion about $v_i = 0$, leading to

$$l(\lambda, \mathbf{x}) = l_0(\gamma, \mathbf{x}) + \sum_{i=1}^{k} \log \left[1 + \frac{h_i(\gamma, \mathbf{x}_i)\theta}{2} + \sum_{m=3}^{\infty} \frac{D_i^{(m)}(\gamma, \mathbf{x}_i)E(V_i^m)\theta^{m/2}}{m!} \right], \tag{6}$$

where

$$D_i^{(m)}(\gamma, \mathbf{x}_i) = \frac{\partial^m L_i(\gamma, \mathbf{x}_i)/\partial\alpha^m}{L_i(\gamma, \mathbf{x}_i)}, \tag{7}$$

with $L_i(\gamma, \mathbf{x}_i) = \prod_{j=1}^{n_i} L_{ij}(\gamma, x_{ij})$ and $l_0(\gamma, \mathbf{x}) = \sum_{i=1}^{k} \log L_i(\gamma, \mathbf{x}_i)$. Moreover, $L_{ij}(\gamma, x_{ij})$ follows from Eq. (4). Denote $s(x_{ij}) = s(x_{ij}, 0) = (y_{ij} - \alpha - \boldsymbol{\beta}_z^T \mathbf{z}_{ij} - \beta_x x_{ij})/\sigma$. It can be shown (Bolfarine and Valença 2005) that the quantity defined as $h_i(\gamma, \mathbf{x}_i) = D_i^{(2)}(\gamma, \mathbf{x}_i)$, can be written as

$$h_i(\gamma, \mathbf{x}_i) = \frac{1}{\sigma^2} \left\{ \left[\sum_{j=1}^{n_i} \left(e^{s(x_{ij})} - \delta_{ij} \right) \right]^2 - \sum_{j=1}^{n_i} e^{s(x_{ij})} \right\}, \tag{8}$$

with $i = 1, \ldots, k$. Let $\mathsf{S}(\lambda; \mathbf{x}) = \partial l(\lambda, \mathbf{x})/\partial\lambda$ be the score function. It can be shown that the element of this vector, corresponding to the parameter θ, $\mathsf{S}_\theta(\lambda; \mathbf{x}) = \partial l(\lambda, \mathbf{x})/\partial\theta$, under H_0, is given by

$$S_\theta(\lambda_0, \mathbf{x}) = \frac{1}{2} \sum_{i=1}^{k} h_i(\gamma, \mathbf{x}_i), \tag{9}$$

with $h_i(\gamma, \mathbf{x}_i)$ given in Eq. (8), and $\lambda_0^T = (\gamma^T, 0)$.

4 Naive tests of homogeneity

We denote by $I(\lambda; \mathbf{x}) = -\partial^2 l(\lambda, \mathbf{x})/\partial\lambda\partial\lambda^T$ the observed information matrix, and by $\Lambda(\lambda; \mathbf{x}) = E[I(\lambda; \mathbf{x})]$ the expected (Fisher) information matrix. Clearly, the above matrices and the score vector $\mathsf{S}(\lambda; \mathbf{x})$ are not available for the model defined by Eqs. (1)–(3) since x_{ij} is not observed. One alternative is to replace the unobserved x_{ij} by the observed w_{ij}, and ignore measurement error. Such procedures are often termed "naive" procedures. Let $\tilde{\lambda}_0^T = (\tilde{\gamma}^T, 0)$ be the naive estimator under H_0 (that is, the solution of $\mathsf{S}(\lambda, \mathbf{w}) = 0$, under $H_0 : \theta = 0$). The naive score statistic could be defined with variance obtained by using the Fisher information matrix. However this matrix is not computable in situations where the data is censored (at random with unspecified distribution) and different naive statistics can be defined depending on the estimated variance of the score statistic.

Denote the "naive" observed information matrix, partitioned according to the parameter vector $\lambda = (\gamma^T, \theta)^T$, by

$$I(\lambda, \mathbf{w}) = \begin{bmatrix} I_{\gamma\gamma}(\lambda, \mathbf{w}) & I_{\gamma\theta}(\lambda, \mathbf{w}) \\ I_{\theta\gamma}(\lambda, \mathbf{w}) & I_{\theta\theta}(\lambda, \mathbf{w}) \end{bmatrix}. \tag{10}$$

According to Valença (2003), two naive score statistics to test the homogeneity hypothesis can be defined, namely,

$$Z_0 = \frac{\frac{1}{2}\sum_{i=1}^{k} h_i(\tilde{\gamma}, \mathbf{w}_i)}{\sqrt{V_0(\tilde{\lambda}_0, \mathbf{w})}}, \qquad \text{and} \qquad Z_H = \frac{\frac{1}{2}\sum_{i=1}^{k} h_i(\tilde{\gamma}, \mathbf{w}_i)}{\sqrt{V_H(\tilde{\lambda}_0, \mathbf{w})}}, \tag{11}$$

where h_i is given in Eq. (8), with x_{ij} replaced by w_{ij}. The estimated variances V_0 and V_H are given by,

$$V_0(\tilde{\lambda}_0, \mathbf{w}) = I_{\theta\theta}(\tilde{\lambda}_0, \mathbf{w}) - I_{\theta\gamma}(\tilde{\lambda}_0, \mathbf{w}) \left(I_{\gamma\gamma}(\tilde{\lambda}_0, \mathbf{w})\right)^{-1} I_{\gamma\theta}(\tilde{\lambda}_0, \mathbf{w})$$

and

$$V_H(\tilde{\lambda}_0, \mathbf{w}) = \frac{1}{4}\sum_{i=1}^{k}(h_i(\tilde{\gamma}, w_i) - \bar{h}(\tilde{\gamma}, \mathbf{w}))^2$$

where $I_{\theta\theta}$, $I_{\theta\gamma}$, $I_{\gamma\theta}$ and $I_{\gamma\gamma}$ are given in Eq. (10), and $\bar{h} = \sum_{i=1}^{k} h_i/k$.

In the uncensored situation, the Fisher information can be computed and in this case Bolfarine and Valença (2005) show that the naive score statistics is given by

$$Z_F = \frac{\left\{\sum_{i=1}^{k}\left[\sum_{j=1}^{n_i}(\mathrm{e}^{\hat{s}(w_{ij})} - 1)\right]^2 - n\right\}}{\sqrt{\sum_{i=1}^{k}(2n_i^2 + 2n_i) - 24n/\pi^2}},$$

where $n = n_1 + \cdots + n_k$ and $\hat{s}(w_{ij}) = (y_{ij} - \hat{\alpha}_0 - \hat{\boldsymbol{\beta}}_{0z}^T \mathbf{z}_{ij} - \hat{\beta}_{0x} w_{ij})/\hat{\sigma}_0$, with $\hat{\alpha}_0$, $\hat{\boldsymbol{\beta}}_{0z}$, $\hat{\boldsymbol{\beta}}_{0x}$ and $\hat{\sigma}_0$ being the naive estimators of α, $\hat{\boldsymbol{\beta}}_z$, β_x and σ.

However, as is well known (Gimenez et al 2000), the naive score function $\mathsf{S}(\lambda, \mathbf{w})$ is biased (i.e., $E[S(\lambda, \mathbf{w})] \neq 0$) leading to inconsistent inferences, with possible implications on the nominal levels of the naive statistics defined above.

References on corrections for testing in models with measurement errors are often related to tests for evaluating the association between the true covariate and the response. Tosteson and Tsiatis (1988) assuming a general structure for measurement errors compare the local power of naive score tests with optimum score tests for association in generalized linear models. Lagakos (1988) study the efficiency loss of naive tests for association in univariate regression models, including the Cox model. Some other references on hypotheses testing in models with measurement errors are given in Carroll et al (1995).

A homogeneity score test for clustered data under generalized linear models with error in covariates (without censoring), is studied in Lin and Carroll (1999). The authors use the SIMEX method (Cook and Stefanski 1994), to propose a general score test to test the null hypothesis that all variance components are zero. An extension of this result is given by Li and Lin (2003), which propose a SIMEX score test for the variance components to test for the within-cluster correlation for clustered survival data. This test is implemented by repeatedly fitting standard Cox models. Here we propose to use the corrected score method to develop a score type statistics to test homogeneity among groups in a Weibull measurement error model with censored observations.

5 The corrected score approach

The corrected score approach for consistent inference in measurement error models was considered in Nakamura (1990) and Gimenez and Bolfarine (1997). The corrected score function $\mathsf{S}^*(\lambda; \mathbf{w}) = \mathsf{S}^*(\lambda; \mathbf{w}, Y)$ is defined as a function whose conditional expectation $E\left[\mathsf{S}^*(\lambda; \mathbf{w}, Y)|\mathbf{x}, Y)\right] = \mathsf{S}(\lambda; \mathbf{x})$. If the corrected information matrix is given by $I^*(\lambda, \mathbf{w}) = -\partial \mathsf{S}^*(\lambda, \mathbf{w})/\partial\lambda$, then the value $\widehat{\lambda}^*$ such that $\mathsf{S}^*(\widehat{\lambda}^*; \mathbf{w}, Y) = 0$, with $I^*(\widehat{\lambda}^*, \mathbf{w})$ positive definite, is called a *corrected estimate* of λ.

5.1 The corrected score vector for the Weibull model

With measurement errors normally distributed, properties of the normal moments generating function can be used to obtain the corrected score vector for the Weibull model in Eqs. (1–3). Specifically, given x_{ij}, the observed w_{ij} follows a normal distribution with mean x_{ij} and variance ϕ which implies, using properties of the normal generating function, that

$$E\left[\exp(\beta_x w_{ij})|x_{ij}\right] = \exp(\beta_x x_{ij} + f) \tag{12}$$

and

$$E\left[w_{ij}\exp(\beta_x w_{ij})|x_{ij}\right] = (x_{ij} + \phi\beta_x)\exp(\beta_x x_{ij} + f), \tag{13}$$

where $f = (\beta_x^2\phi)/2\sigma^2$.

The corrected score vector can be obtained directly by using the naive score vector and correcting it by using Eq. (12) and Eq. (13) above. The element of the naive score vector corresponding to θ, under H_0 is given in Eq. (9) with x_{ij} replaced by w_{ij}. Closed form expressions for all the elements of the corrected score vector are given in the Appendix. An alternative way of obtaining the corrected score vector is to obtain first, the corrected log-likelihood function, when it is possible. In this model it can be obtained by correcting directly the naive likelihood obtained through Eq. (6) with the use of expressions Eq. (12) and Eq. (13). The resulting expression is given by

$$l^*(\lambda, \mathbf{w}) = l_0^*(\gamma, \mathbf{w}) + \sum_{i=1}^{k} \log\left[1 + \frac{h_i^*(\gamma, w_i)\theta}{2} + \sum_{m=3}^{\infty} \frac{D_i^{*(m)}(\gamma, w_i)\theta^{m/2} E(V_i^m)}{m!}\right], \tag{14}$$

where

$$l_0^*(\gamma, \mathbf{w}) = \sum_{i=1}^{k}\sum_{j=1}^{n_i} \left\{\delta_{ij}\left[s(w_{ij}) - \log\sigma\right] - \exp(s(w_{ij}) - f)\right\},$$

and

$$h_i^*(\gamma, w_i) = \frac{1}{\sigma^2}\left\{\left[\sum_{j=1}^{n_i}\left(\mathrm{e}^{s(w_{ij})-f} - \delta_{ij}\right)\right]^2 - \sum_{j=1}^{n_i} \mathrm{e}^{s(w_{ij})-f} - F_i\right\}, \tag{15}$$

with

$$s(w_{ij}) = \frac{y_{ij} - \alpha - \beta_z^T \mathbf{z}_{ij} - \beta_x w_{ij}}{\sigma}, \quad f = \frac{\beta_x^2 \phi}{2\sigma^2}$$

and

$$F_i = \sum_{j=1}^{n_i}\left[\exp(2s(w_{ij}) - 2f) - \exp(2s(w_{ij}) - 4f)\right].$$

Moreover, the quantity $D_i^{*(m)}(\gamma, w_i)$ is such that

$$E[D_i^{*(m)}(\gamma, w_i)|Y, x_i] = D_i^{(m)}(\gamma, x_i),$$

with $D_i^{(m)}$ given in Eq. (7). Although an analytic expression for $D_i^{*(m)}$ is not easily found, it is really not necessary in obtaining the score statistic (Valença 2003).

The corrected score under the null hypothesis is obtained by using the corrected log-likelihood function l^* in Eq. (14), that is, $\mathsf{S}^*(\lambda_0; \mathbf{w}) = \partial l^*(\lambda, \mathbf{w})/\partial\lambda|_{\lambda=\lambda_0}$. The corrected information matrix under H_0 is defined by

$$I^*(\lambda_0, \mathbf{w}) = -\left(\frac{\partial \mathsf{S}^*(\lambda; \mathbf{w})}{\partial\lambda}\right)|_{\lambda=\lambda_0}. \tag{16}$$

Closed form for the elements of this matrix are given in the Appendix.

5.2 Score tests based on the corrected score

Gimenez et al. (2000) consider the development of hypothesis testing statistics based on the corrected score function, using an additive model, and investigate the asymptotic distribution of the tests in the situations where the parameter is in a open subset of the parametric space.

The following theorem describes the main asymptotic results related to the corrected score test. We start defining the following matrices:

$$\Gamma_k^*(\lambda, \mathbf{w}) = \sum_{i=1}^{k} E\left[\mathsf{S}_i^*(\lambda, \mathbf{w}_i)\mathsf{S}_i^{*T}(\lambda, \mathbf{w}_i)\right] \quad \text{and} \quad \Lambda_k^*(\lambda, \mathbf{w}) = E\left[I^*(\lambda, \mathbf{w})\right].$$

Suppose that there are positive matrices $\Gamma^*(\lambda)$ and $\Lambda^*(\lambda)$ such that as, $k \to \infty$,

$$\frac{1}{k}\Gamma_k^*(\lambda, \mathbf{w}) \to \Gamma^*(\lambda) \quad \text{and} \quad \frac{1}{k}\Lambda_k^*(\lambda, \mathbf{w}) \to \Lambda^*(\lambda). \tag{17}$$

Define

$$\Sigma^*(\lambda) = \Lambda^{*-1}(\lambda)\Gamma^*(\lambda)\Lambda^{*-1}(\lambda). \tag{18}$$

We consider the above matrices partitioned according to the parameter vector $\lambda = (\gamma^T, \theta)^T$, as in Eq. (10).

Theorem 5.1 *Consider the hypothesis $H_0 : \theta = \theta_0$ against the alternative $H_1 : \theta \neq \theta_0$. Let $\lambda_0 = (\gamma, \theta_0)$ the parameter under the hypothesis H_0, with $\widehat{\lambda}_0^*$ representing the solution to the equation $\mathsf{S}^*(\lambda, \mathbf{w}) = 0$, under H_0. Define the statistic Q_c as*

$$Q_c = \frac{[\mathsf{S}_\theta^*(\widehat{\lambda}_0^*, \mathbf{w})]^2}{k\widehat{V}^*(\widehat{\lambda}_0^*)},$$

where

$$\widehat{V}^*(\lambda) = \left[V_F^*(\lambda)\right]^T \Sigma_{\theta\theta}^*(\lambda) V_F^*(\lambda) = \left[V_F^*(\lambda)\right]^2 \Sigma_{\theta\theta}^*(\lambda),$$

with

$$V_F^*(\lambda,) = \Lambda_{\theta\theta}^*(\lambda) - \Lambda_{\theta\gamma}^*(\lambda)\left\{\Lambda_{\gamma\gamma}^*(\lambda)\right\}^{-1}\Lambda_{\gamma\theta}^*(\lambda),$$

where the elements given above correspond to the elements of the partitioned matrices given in Eqs. (17) and (18), partitioned as in Eq. (10). Then, under appropriate regularity conditions it follows, under H_0, that

$$Q_c \to^D \chi^2_{(1)}.$$

The proof of this theorem and some other related results can be found in Gimenez et al. (2000). Note that we can not use directly Theorem 5.1 to test the hypothesis $H_0 : \theta = 0$ against the one-sided alternative $H_1 : \theta > 0$, which is our main goal. Besides, since θ is a variance, the null hypothesis puts the parameter on the boundary of the parametric space.

Moran (1971) and Self and Liang (1987) deal with boundary problems in hypothesis testing using likelihood ratio tests. Vu and Zhou (1997) derive the nonstandard asymptotic distribution of a generalization of the likelihood ratio test, representing extensions of less general results in Moran (1971), Chant (1974) and Self and Liang (1987) by covering a large class of estimation problems which allows sampling from nonidentically distributed random variables including, for example, models with covariates or incidental parameters, as is the case with the functional model we are considering. The equivalence between likelihood ratio and score statistics for one sided situations when the parametric space is open has been established in Silvapulle and Silvapulle (1995) (see also Paula and Artes 2000). We assume that this is the case with the situation considered in this paper. We investigate this asymptotic distribution through simulation studies in moderate and small sample situations for the model considered in this paper.

5.3 The proposed corrected score test of homogeneity

Consider the hypothesis $H_0 : \theta = 0$ against $H_1 : \theta > 0$ with the model defined in Sect. 2. Based on the results given in Theorem 5.1, we define the statistics Z_C and Q as:

$$Z_C = \frac{\frac{1}{2}\sum_{i=1}^{k} h_i^*(\hat{\gamma}^*, w_i)}{\sqrt{V_C(\hat{\lambda}_0^*, \mathbf{w})}}, \quad \text{and} \quad Q = \begin{cases} 0 & \text{if } Z_C \le 0, \\ Z_C^2 & \text{if } Z_C > 0, \end{cases}$$

where $\hat{\lambda}_0^* = (\hat{\gamma}^{*T}, 0)^T$, is the corrected estimate under the null hypothesis (solution of $\mathsf{S}^*(\lambda; \mathbf{w}) = 0$, under $H_0 : \theta = 0$) and h_i^* is given in Eq. (15). Considering the matrices partitioned according to $\lambda = (\gamma^T, \theta)^T$, V_C is defined as

$$V_C(\lambda_0, \mathbf{w}) = \left[V_0^*(\lambda_0, \mathbf{w})\right]^2 G_{\theta\theta}^*(\lambda_0, \mathbf{w}),$$

where

$$V_0^*(\lambda_0, \mathbf{w}) = I_{\theta\theta}^*(\lambda_0, \mathbf{w}) - I_{\theta\gamma}^*(\lambda_0, \mathbf{w}) \left\{I_{\gamma\gamma}^*(\lambda_0, \mathbf{w})\right\}^{-1} I_{\gamma\theta}^*(\lambda_0, \mathbf{w}), \tag{19}$$

with $I_{\theta\theta}^*$, $I_{\theta\gamma}^*$, $I_{\gamma\theta}^*$ and $I_{\gamma\gamma}^*$ being elements of I^* given in Eq. (16). $G_{\theta\theta}^*$ is the element corresponding to θ in the matrix

$$G^*(\lambda_0, \mathbf{w}) = I^{*-1}(\lambda_0, \mathbf{w})\widehat{\Gamma}^*(\lambda_0, \mathbf{w})I^{*-1}(\lambda_0, \mathbf{w}),$$

with

$$\widehat{\Gamma}^*(\lambda_0, \mathbf{w}) = \sum_{i=1}^{k} \mathsf{S}_i^*(\lambda_0, \mathbf{w}_i)\mathsf{S}_i^T(\lambda_0, \mathbf{w}_i).$$

Under H_0, we consider that the limiting distribution of Q, as $k \to \infty$, can be approximated by a mixture of chi-squared distributions, $1/2\chi_{(0)}^2 + 1/2\chi_{(1)}^2$, where χ_0^2 denotes the degenerate distribution at the origin. This procedure produces the same critical region obtained with the unilateral test using the statistic Z_C which rejects the null hypothesis for large positive values of this statistic.

We can use the sandwich structure of the variance of Z_C to define another naive statistic, $Z_{\text{naive}} = 1/2 \sum_{i=1}^{k} h_i(\tilde{\gamma}, w_i)/(V_{\text{naive}}(\tilde{\lambda}_0, \mathbf{w}))^{1/2}$, where $\tilde{\lambda}_0 = (\tilde{\gamma}^T, 0)^T$ is the naive estimate under H_0, $h_i(\tilde{\gamma}, w_i)$ is given in Eq. (8), with x_{ij} replacing w_{ij} and V_{naive} is obtained similarly to V_C, but using the usual observed information matrix and the sandwich estimator instead of the corrected functions.

6 Simulation study

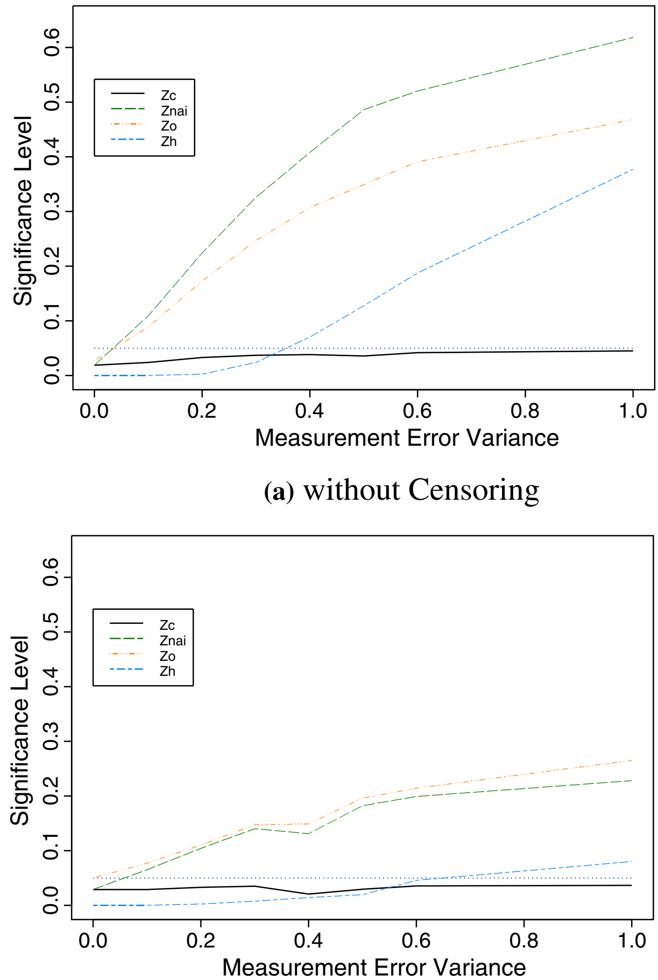
A simulation study was conducted to compare the performance of the proposed test based on the corrected score Z_C, with the naive testing statistics Z_0 and Z_H given in Eq. (11) and Z_{naive} defined in the previous section. Note that in the case of $\phi = 0$ the naive statistic $Z_{\text{naive}} = Z_C$. The log-survival times Y_{ij} were generated within each group under a log-linear Weibull model given in Sect. 2, with two covariates, one (z_{ij}) measured without error, generated according to the $N(3, 1)$ and the true (unobserved) (x_{ij}) generated according to the $N(2, 1)$. The covariate observed with error is $w_{ij} = x_{ij} + \phi^{1/2}\dot{\eta}_{ij}$, where ϕ is the (measurement) error variance and $\dot{\eta}_{ij}$ is generated according to the $N(0, 1)$. Parameter values were taken as $\alpha = 0.5$, $\beta_z = 0.8$ and $\beta_x = 1$. We took $\sigma = 0.75$ (shape parameter for the Weibull model), corresponding to a situation of an increasing hazard function ($\sigma < 1$) as is typically encountered in practice. The random effect V_{ij} are taken as independent and identically distributed (i.i.d) $N(0, 1)$. The censoring times C_{ij} were generated as i.i.d uniform on $U(0, \psi)$. We consider uncensored samples and sample with 50% censoring, which is achieved by conveniently choosing ψ. Three different sample sizes were considered with groups of sizes k=25, k=50 and k=100, with n_i=5 in all cases. The nominal significance level was taken as 5%. Under each parameter combination, test sizes were computed based on 1,000 simulated samples which were executed using subroutine BFGS in program Ox (Doornik 2001) to do estimation under the null hypothesis. S-plus subroutines were used to present the results graphically.

Table 1 shows the empirical (simulated) significance levels for the statistics described above. Notice that without measurement errors (ϕ=0), the naive statis-

Table 1 Simulated levels of corrected (Z_C) and naive (Z_0, Z_H, Z_{naive}) tests of homogeneity for different sample sizes and different values of the variance of the measurement error with and without censoring. Results based on 1,000 simulated samples.

		0% Censored				50% Censored			
ϕ	k	Z_c	Z_{naive}	Z_o	Z_H	Z_c	Z_{naive}	Z_o	Z_H
	25	0.027	0.027	0.057	0	0.021	0.021	0.055	0
0	50	0.024	0.024	0.048	0	0.019	0.019	0.045	0
	100	0.029	0.029	0.030	0	0.029	0.029	0.039	0
	25	0.019	0.057	0.087	0.001	0.013	0.038	0.087	0
0.2	50	0.032	0.135	0.123	0.001	0.034	0.082	0.112	0.001
	100	0.033	0.224	0.173	0.002	0.033	0.104	0.110	0.002
	25	0.014	0.096	0.111	0.007	0.018	0.052	0.116	0.002
0.4	50	0.029	0.213	0.177	0.022	0.016	0.098	0.131	0.009
	100	0.038	0.408	0.307	0.065	0.021	0.131	0.149	0.013
	25	0.015	0.122	0.117	0.005	0.002	0.049	0.110	0.007
0.6	50	0.035	0.238	0.181	0.036	0.027	0.098	0.144	0.017
	100	0.042	0.520	0.391	0.173	0.035	0.199	0.214	0.042

tics Z_0, presents simulated levels closest to the nominal levels. On the other hand, as ϕ increases, the naive statistics tend to present empirical levels much higher than the nominal levels. On the contrary, the correct statistics presents a much better behaviour, specially as k increases. As ϕ increases, the erratic behaviour of all tests except Z_C can also be depicted from Fig. 1, which is also based on 1,000 simulated samples generated according to the population described above with 100 groups and a sample n_i=5 from each group. We can evaluate in a detailed way the effect of the parameter ϕ on the simulated levels of the tests. As noted above, it is clear that the naive tests yields simulated levels very far from the nominal levels (5%) as ϕ



(a) without Censoring

(b) 50% censored

Fig. 1 Simulated levels of corrected (Z_C) and naive (Z_0, Z_H, Z_{naive}) tests of homogeneity for increasing values of the variance of the measurement error (results based on 1,000 simulated samples) increases, while the corrected testing statistics Z_C presents simulated (empirical) levels (sizes) quite close to the nominal levels. Although censoring has the effect of reducing the level of the tests, in general the use of the corrected testing statistics Z_C leads to reasonable improvement in the level of the test.

7 Final discussion

In this paper we discuss homogeneity tests for Weibull mixed models with measurement errors. We use the correct score approach for deriving the corrected statistics. Closed form expressions are obtained for the corrected score vector and for the corrected observed information matrix. In the process we also have obtained the corrected likelihood for the Weibull mixed model with measurement errors which can also be used for obtaining the corrected score and observed information matrices. Simulation studies have demonstrated that the corrected score statistics behaves better than alternative statistics that can be defined in terms of closeness to the nominal levels.

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Appendix 1 The corrected score for the Weibull mixed model

Appendix 1.1: Corrected score vector

For the log-linear Weibull model defined in Sect. 2, the corrected score vector $\mathsf{S}^*(\lambda_0, \mathbf{w})$, partitioned according to $\lambda = (\alpha, \boldsymbol{\beta}_z^T, \beta_x, \sigma, \theta)$ obtained by differentiating the corrected log-likelihood in Eq. (14) is given by the following partitions:

$$\mathsf{S}^*_\alpha(\lambda_0, \mathbf{w}) = \frac{1}{\sigma}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\left\{\mathrm{e}^{s(w_{ij})-f} - \delta_{ij}\right\};$$

$$\mathsf{S}^*_{\beta_z}(\lambda_0, \mathbf{w}) = \frac{1}{\sigma}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\left\{\mathrm{e}^{s(w_{ij})-f} - \delta_{ij}\right\}\mathbf{z}_{ij};$$

$$\mathsf{S}^*_{\beta_x}(\lambda_0, \mathbf{w}) = \frac{1}{\sigma}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\left\{\left[\mathrm{e}^{s(w_{ij})-f} - \delta_{ij}\right]w_{ij} + \frac{\phi\beta_x}{\sigma}\mathrm{e}^{s(w_{ij})-f}\right\}; \tag{20}$$

$$\mathsf{S}^*_\sigma(\lambda_0, \mathbf{w}) = \frac{1}{\sigma}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\left\{s(w_{ij})\mathrm{e}^{s(w_{ij})-f} - \delta_{ij}\left(1 + s(w_{ij})\right) - 2f\mathrm{e}^{s(w_{ij})-f}\right\};$$

$$\mathsf{S}^*_\theta(\lambda_0, \mathbf{w}) = \frac{1}{2}\sum_{i=1}^{k}h_i^*(\gamma, w_i)$$

where

$$h^*(\gamma, w_i) = \frac{1}{\sigma^2}\sum_{i=1}^{k}\left\{\left[\sum_{j=1}^{n_i}\left(e^{s(w_{ij})-f} - \delta_{ij}\right)\right]^2 - \sum_{j=1}^{n_i} e^{s(w_{ij})-f} - \sum_{j=1}^{n_i} e^{2s(w_{ij})-2f} + \sum_{j=1}^{n_i} e^{2s(w_{ij})-4f}\right\}. \quad (21)$$

with $s(w_{ij}) = (y_{ij} - \alpha - \boldsymbol{\beta}_z^T \mathbf{z}_{ij} - \beta_x w_{ij})/\sigma$, and $f = (\beta_x^2 \phi)/2\sigma^2$.

Appendix 1.2: Corrected observed information matrix

Let $\boldsymbol{\beta} = (\alpha, \boldsymbol{\beta}_z^T, \beta_x)^T$ and consider the corrected observed information matrix I^* in Eq. (16), partitioned according to $\lambda = (\boldsymbol{\beta}^T, \sigma, \theta)^T$. The partitions of $I^*(\hat{\lambda}_0^*, \mathbf{w})$, being $\widehat{\lambda}_0^* = (\hat{\alpha}, \hat{\boldsymbol{\beta}}_z^T, \hat{\beta}_x, \hat{\sigma}, 0)^T$ the solution of $S^*(\lambda, \mathbf{w}) = 0$, under H_0 are given by

$$I^*_{\theta\theta}(\widehat{\lambda}_0^*, \mathbf{w}) \simeq \frac{1}{4}\sum_{i=1}^{k}\left[h_i^*(\widehat{\gamma}, w_i)\right]^2,$$

$$I^*_{\sigma\sigma}(\hat{\lambda}_0^*) = \frac{1}{\hat{\sigma}^2}\left[\sum_{i=1}^{k}\sum_{j=1}^{n_i}\hat{s}^{*2}(w_{ij})e^{\hat{s}(w_{ij})-\hat{f}} + r(1-2\hat{f})\right],$$

$$I^*_{\theta\sigma}(\widehat{\lambda}_0^*, \mathbf{w}) = \frac{1}{2\hat{\sigma}^3}\sum_{i=1}^{k}\left\{\left[2\sum_{j=1}^{n_i}\left(e^{\hat{s}^*(w_{ij})-\hat{f}} - \delta_{ij}\right) - 1\right]\left[\sum_{j=1}^{n_i}\hat{s}^*(w_{ij})e^{\hat{s}(w_{ij})-\hat{f}}\right] + 2\hat{\sigma}^2 h_i^*(\widehat{\gamma}, w_i)\right\} - 2\sum_{i=1}^{k}\sum_{j=1}^{n_i}\left(\hat{s}^*(w_{ij})e^{2\hat{s}(w_{ij})-2\hat{f}} - (\hat{s}(w_{ij}) - 4\hat{f})e^{2\hat{s}(w_{ij})-4\hat{f}}\right),$$

$$I^*_{\boldsymbol{\beta}\theta}(\hat{\lambda}_0^*, \mathbf{w}) = \tfrac{1}{2\hat{\sigma}^3}\sum_{i=1}^{k}\begin{bmatrix} J_i \sum_{j=1}^{n_i} e^{\hat{s}(w_{ij})-\hat{f}} - \sum_{j=1}^{n_i} M_{ij} \\ J_i \sum_{j=1}^{n_i} \mathbf{z}_{ij} e^{\hat{s}(w_{ij})-\hat{f}} - \sum_{j=1}^{n_i} \mathbf{z}_{ij} M_{ij} \\ J_i \sum_{j=1}^{n_i} \hat{w}_{ij}^* e^{\hat{s}(w_{ij})-\hat{f}} - \sum_{j=1}^{n_i} \hat{w}_{ij}^* M_{ij} + \frac{2\hat{\beta}_x\phi}{\hat{\sigma}}\sum_{j=1}^{n_i} e^{2\hat{s}(w_{ij})-4\hat{f}} \end{bmatrix},$$

$$I^*_{\boldsymbol{\beta}\boldsymbol{\beta}}(\hat{\lambda}^*_0, \mathbf{w}) = \frac{1}{\hat{\sigma}^2}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\begin{bmatrix} e^{\hat{s}(w_{ij})-\hat{f}} & \mathbf{z}^T_{ij}e^{\hat{s}(w_{ij})-\hat{f}} & \hat{w}^*_{ij}e^{\hat{s}(w_{ij})-\hat{f}} \\ \mathbf{z}_{ij}e^{\hat{s}(w_{ij})-\hat{f}} & \mathbf{z}_{ij}\mathbf{z}^T_{ij}e^{\hat{s}(w_{ij})-\hat{f}} & \mathbf{z}_{ij}\hat{w}^*_{ij}e^{\hat{s}(w_{ij})-\hat{f}} \\ \hat{w}^*_{ij}e^{\hat{s}(w_{ij})-\hat{f}} & \mathbf{z}_{ij}\hat{w}^*_{ij}e^{\hat{s}(w_{ij})-\hat{f}} & \hat{w}^{*2}_{ij}e^{\hat{s}(w_{ij})-\hat{f}} - \frac{\phi r}{n} \end{bmatrix},$$

$$I^*_{\boldsymbol{\beta}\sigma}(\hat{\lambda}^*_0) = \frac{1}{\hat{\sigma}^2}\sum_{i=1}^{k}\sum_{j=1}^{n_i}\begin{bmatrix} \hat{s}^*(w_{ij})e^{\hat{s}(w_{ij})-\hat{f}} \\ \mathbf{z}_{ij}\hat{s}^*(w_{ij})e^{\hat{s}(w_{ij})-\hat{f}} \\ \hat{w}^*_{ij}\hat{s}^*(w_{ij})e^{\hat{s}(w_{ij})-\hat{f}} + \frac{r\phi\hat{\beta}_x}{\hat{\sigma}} \end{bmatrix},$$

where $\hat{s}(w_{ij}) = (y_{ij} - \hat{\alpha} - \hat{\boldsymbol{\beta}}^T_z\mathbf{z}_{ij} - \hat{\beta}_x w_{ij})/\hat{\sigma}$, $\widehat{f} = f(\widehat{\lambda^*_0}) = (\widehat{\beta^2_x\phi})/(2\hat{\sigma}^2)$, $\hat{s}^*(w_{ij}) = \hat{s}(w_{ij}) - 2\hat{f}$ and $\hat{w}^*_{ij} = w_{ij} + (\widehat{\beta}_x\phi/\hat{\sigma})$, and with r_i representing failure numbers in group i, to a total number of $r = r_1+\cdots+r_k$ failures. Besides, to simplify the expressions in partition $I^*_{\beta\theta}$ given below, we use the following notation

$$J_i = 2\sum_{j=1}^{n_i}(e^{\hat{s}(w_{ij})-\hat{f}} - \delta_{ij}) \quad M_{ij} = e^{\hat{s}(w_{ij})-\hat{f}} + 2e^{2\hat{s}(w_{ij})-2\hat{f}} - e^{2\hat{s}(w_{ij})-4\hat{f}}.$$

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ERRATUM

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