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CONFIDENCE INTERVAL OF PARAMETERS IN MULTIRESPONSE MULTIPREDICTOR SEMIPARAMETRIC REGRESSION MODEL FOR LONGITUDINAL DATA BASED ON TRUNCATED SPLINE ESTIMATOR

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Abstract: In this paper, we provide a theoretical discussion on estimating confidence interval of parameters in a multiresponse multipredictor semiparametric regression (MMSR) model for longitudinal data. The MMSR model consists of two components namely a parametric component and a nonparametric component. In consequently, estimating the MMSR model is equivalent to estimating the parametric and nonparametric components. Estimating the parametric component is equivalent to estimating parameters of the model, while estimating the nonparametric component is estimating unknown smooth function. In this paper, we estimate the parametric and nonparametric components using a weighted least square method and a smoothing technique namely truncated spline, respectively. Next, we estimate the confidence interval of parameters in the MMSR model using pivotal quantity and Lagrange multiplier functions. The results of this study can be applied to the Covid-19 data that is to model the case growth rate

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(CGR) and case fatality rate (CFR) of Covid-19 which are influenced by many variables including comorbid, age, gender, temperature, self-isolation, isolation in hospital, and others.

Keywords: confidence interval; Covid-19; longitudinal data; MMSR model; truncated spline estimator.

2010 AMS Subject Classification: 62F10, 62G05, 62G08.

1. INTRODUCTION

Regression analysis is one of the statistical methods used to explain the functional relationship between response and predictor variables. The pattern of functional relationships between response variables and predictor variables in the regression model can be estimated using two approaches, namely parametric regression model and nonparametric regression model approaches. The parametric regression model approach is used if the functional relationship between the response and predictor variables is assumed to follow a specific form, for examples linear, quadratic, cubic, etc. In contrast, the nonparametric regression model approach is used if the functional relationship between the response variable and the predictor does not assume a specific form of function. In the nonparametric regression, the estimation of the regression function is based on observational data using smoothing techniques, for examples local linear estimators [1–6], local polynomial estimators [7,8], kernel estimators [9–11], and spline estimators [9–32]. One of very popular smoothing techniques is splines, for examples least square spline [27–29], penalized spline [22,24,25,32], truncated spline [14,26], and smoothing spline [9–13,15–21,23,26,30,31].

Furthermore, if we combine the parametric regression model and the nonparametric regression, we will obtain a new regression model called as semiparametric regression model [33]. There are several studies that used some estimators to estimate the regression function of the semiparametric regression model, for examples local linear estimator [34], least square spline estimator [35–37], truncated spline estimator [38–41], and smoothing spline estimator [42–44]. But, the studies previously mentioned used cross-sectional data, whereas problems in everyday life often want to know the changes in the subjects studied on an ongoing basis. For this reason, research using longitudinal data is needed. Several studies on the use of longitudinal data are [14,24,32] that applied the nonparametric regression model based on penalized spline estimator and [37] that applied the semiparametric regression model based on least square spline estimator.

An essential part of statistical inference is a confidence interval of model parameters. The statistical size of the population can be found through the confidence interval because the confidence interval presents the range of possible values in it [12,33,44]. In semiparametric regression model, the confidence interval of the model parameters can be used to determine the predictor variables that significantly affect the response variable. The confidence interval of the model parameters, if it contains a value of zero, then the predictor variable has no significant effect on the response variable. Researches on confidence intervals are [2,5] that used nonparametric local linear estimators, [2] that used nonparametric smoothing spline estimator, [34] that used semiparametric local linear estimator, [35,36] that used semiparametric least square spline estimators, and [40,41,44] that used semiparametric truncated spline estimators.

Although those researches on confidence intervals have been done by previous researchers, but those researches were applied to cross-section data and for single response and single predictor semiparametric regression models only. Many problems in real life involve many response variables and predictor variables or multi-response and multi-predictors. Therefore, this study aims to discuss theoretically how to estimate the confidence interval of the semiparametric multi-response multi-predictor regression model for longitudinal data using truncated spline estimator in which in the future the results of this study can be applied to data on the growth and fatality rate of Covid-19 in Indonesia. The truncated spline regression approach has several advantages, including being easier in mathematical calculations, and the interpretation of the model is almost the same as in parametric regression. The truncated spline is one type of polynomial slices that has segmented properties. By having segmented properties, it results in a higher level of flexibility compared to ordinary polynomial pieces.

2. PRELIMINARIES

In the semiparametric regression model, the parametric components follow a specific pattern, and the nonparametric components in the form of functional relationships that do not assume certain functions. Given a pair of longitudinal data $(y_i^{(r)}, x_{ip}, t_{iq})$ where $r = 1,2,...,R$; $i = 1,2,...,n$;

$p=1,2,...,a$; $q=1,2,...,b$ which satisfies the MMSR model as follows:

$$1 \qquad y_i^{(r)} = \sum_{p=0}^{a} \beta_p^{(r)} x_{ip} + \sum_{q=1}^{b} g_q^{(r)}(t_{iq}) + \varepsilon_i^{(r)}$$

where y_i^r is the r-th response variable, the i-th subject, $\sum_{p=0}^{a} \beta_p^{(r)} x_{ip}$ is a parametric component that contains parameters β and *x* variable. $\sum_{q=1}^{b} g_q^{(r)}(t_{iq})$ is a nonparametric component which is the number of functions of the variable t , and $\varepsilon_i^{(r)}$ is a random error.

Next, based on equation (1), the multi-predictor multi-response semiparametric regression model on longitudinal data for the *r*-th response, *i*-th subject and *s*-time can be rewritten as follows:

$$2 \qquad y_{is}^{(r)} = \beta_0^{(r)} + \sum_{p=1}^{a} \beta_p^{(r)} x_{ips} + \sum_{q=1}^{b} g_q^{(r)}(t_{iqs}) + \varepsilon_{is}^{(r)}$$

where $g_q^{(r)}$ is approximated by a nonparametric regression approach based on a Spline Truncated estimator of order $dq^{(r)}$ with knots $\varphi_1, \varphi_2, ..., \varphi_{K_q^{(r)}}$ points, so that equation (2) can be rewritten as:

$$(3) \qquad y_{is}^{(r)} = \beta_0^{(r)} + \sum_{p=1}^{a} \beta_p^{(r)} x_{ips} + \sum_{q=1}^{b} \left(\alpha_{0q}^{(r)} + \sum_{d=1}^{D^{(r)}} \alpha_{dq}^{(r)} t_{iqs}^{d} + \sum_{k=1}^{K^{(r)}} \alpha_{D_q^{(r)}+kq}^{(r)} (t_{iqs} - \varphi_{kq})_+^{D_q^{(r)}} \right) + \varepsilon_{is}^{(r)}$$

where $(t_{iqs} - \varphi_{kq})_+^{D_q^{(r)}}$ satisfies the following equation:

$$(4) \qquad (t_{iqs} - \varphi_{kq})_+^{D_q^{(r)}} = \begin{cases} (t_{iqs} - \varphi_{kq})^{D_q^{(r)}} & , t_{iqs} \geq \varphi_{kq} \\ 0 & , t_{iqs} < \varphi_{kq} \end{cases}$$

Hence, in general, equation (2) can be rewritten as follows:

$$(5) \qquad \underset{\sim}{y} = \mathbf{X}\underset{\sim}{\beta} + \mathbf{Z}\underset{\sim}{\alpha} + \underset{\sim}{\varepsilon}$$

Furthermore, the parameters of the MMSR model of longitudinal data based on the truncated spline estimator can be estimated using a weighted least square (WLS) method by minimizing the number of weighted squared error.

3. Main Results

To obtain the estimation of the MMSR model of longitudinal data, we first express the MMSR model expressed in equation (5) as follows:

(6) $\underset{\sim}{y} - \mathbf{X}\underset{\sim}{\beta} - \mathbf{Z}\underset{\sim}{\alpha} = \underset{\sim}{\varepsilon}, \;\; \underset{\sim}{\varepsilon} \sim N(\underset{\sim}{0}, \mathbf{V})$

where $\underset{\sim}{y} = (\underset{\sim}{y}^{(1)}, \underset{\sim}{y}^{(2)}, ..., \underset{\sim}{y}^{(R)})^T$ in which it components are

$$\underset{\sim}{y}^{(1)} = \begin{bmatrix} y_{11}^{(1)} & y_{12}^{(1)} & \dots & y_{1m_1}^{(1)} & y_{21}^{(1)} & y_{22}^{(1)} & \dots & y_{2m_2}^{(1)} & \dots & y_{n1}^{(1)} & y_{n2}^{(1)} & \dots & y_{nm_n}^{(1)} \end{bmatrix}^T$$

$$\underset{\sim}{y}^{(2)} = \begin{bmatrix} y_{11}^{(2)} & y_{12}^{(2)} & \dots & y_{1m_1}^{(2)} & y_{21}^{(2)} & y_{22}^{(2)} & \dots & y_{2m_2}^{(2)} & \dots & y_{n1}^{(2)} & y_{n2}^{(2)} & \dots & y_{nm_n}^{(2)} \end{bmatrix}^T$$

$$\vdots$$

$$\underset{\sim}{y}^{(R)} = \begin{bmatrix} y_{11}^{(R)} & y_{12}^{(R)} & \dots & y_{1m_1}^{(R)} & y_{21}^{(R)} & y_{22}^{(R)} & \dots & y_{2m_2}^{(R)} & \dots & y_{n1}^{(R)} & y_{n2}^{(R)} & \dots & y_{nm_n}^{(R)} \end{bmatrix}^T$$

where $\mathbf{X} = \begin{bmatrix} \mathbf{X}^{(1)} & 0 & \cdots & 0 \\ 0 & \mathbf{X}^{(2)} & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & \mathbf{X}^{(R)} \end{bmatrix}$; $\underset{\sim}{\beta} = (\beta_0^{(1)}\ \beta_1^{(1)} \cdots \beta_a^{(1)}\ \beta_0^{(2)}\ \beta_1^{(2)} \cdots \beta_a^{(2)} \cdots \beta_0^{(R)}\ \beta_1^{(R)} \cdots \beta_a^{(R)})$;

$$\mathbf{X}^{(r)} = \begin{bmatrix} 1 & x_{111} & \cdots & x_{1a1} \\ 1 & x_{112} & \cdots & x_{1a2} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{11m_1} & \cdots & x_{1am_1} \\ 1 & x_{211} & \cdots & x_{2a1} \\ 1 & x_{212} & \cdots & x_{2a2} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{21m_2} & \cdots & x_{2am_2} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{n11} & \cdots & x_{na1} \\ 1 & x_{n12} & \cdots & x_{na2} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{n1m_n} & \cdots & x_{nam_n} \end{bmatrix}; \;\; \mathbf{Z} = \begin{bmatrix} \mathbf{Z}^{(1)} & 0 & \cdots & 0 \\ 0 & \mathbf{Z}^{(2)} & \cdots & 0 \\ 0 & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \mathbf{Z}^{(R)} \end{bmatrix}; \;\; \mathbf{Z}^{(r)} = \begin{bmatrix} 1 & Z_1^{(r)} & Z_2^{(r)} & \cdots & Z_b^{(r)} \end{bmatrix}$$

$$Z_q^{(r)} = \begin{bmatrix} t_{1q1}^{1} & t_{1q1}^{2} & \cdots & t_{1q1}^{D_q^{(r)}} & \left(t_{1q1}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{1q1}-\varphi_{K^{(2)}q}\right)_+^{D_q^{(r)}} \\ t_{1q2}^{1} & t_{1q2}^{2} & \cdots & t_{1q2}^{D_q^{(r)}} & \left(t_{1q2}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{1q2}-\varphi_{K^{(2)}q}\right)_+^{D_q^{(r)}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ t_{1qm_1}^{1} & t_{1qm_1}^{2} & \cdots & t_{1qm_1}^{D_q^{(r)}} & \left(t_{1qm_1}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{1qm_1}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ t_{2q1}^{1} & t_{2q1}^{2} & \cdots & t_{2q1}^{D_q^{(r)}} & \left(t_{2q1}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{2q1}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ t_{2q2}^{1} & t_{2q2}^{2} & \cdots & t_{2q2}^{D_q^{(r)}} & \left(t_{2q2}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{2q2}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ t_{2qm_2}^{1} & t_{2qm_2}^{2} & \cdots & t_{2qm_2}^{D_q^{(r)}} & \left(t_{2qm_2}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{2qm_2}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \cdots & \vdots \\ t_{nq1}^{1} & t_{nq1}^{2} & \cdots & t_{nq1}^{D_q^{(r)}} & \left(t_{nq1}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{nq1}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ t_{nq2}^{1} & t_{nq2}^{2} & \cdots & t_{nq2}^{D_q^{(r)}} & \left(t_{nq2}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{nq2}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ t_{nqm_n}^{1} & t_{nqm_n}^{2} & \cdots & t_{nqm_n}^{D_q^{(r)}} & \left(t_{nqm_n}-\varphi_{1q}\right)_+^{D_q^{(r)}} & \cdots & \left(t_{nqm_n}-\varphi_{K^{(r)}q}\right)_+^{D_q^{(r)}} \end{bmatrix};$$

$\underset{\sim}{\varepsilon} = \left[\underset{\sim}{\varepsilon}^{(1)} \quad \underset{\sim}{\varepsilon}^{(2)} \quad \cdots \quad \underset{\sim}{\varepsilon}^{(R)}\right]^T$; and $\underset{\sim}{\varepsilon}^{(r)} = \left[\varepsilon_{11}^{(r)} \quad \varepsilon_{12}^{(r)} \quad \cdots \quad \varepsilon_{1m_1}^{(r)} \quad \cdots \quad \varepsilon_{n1}^{(r)} \quad \varepsilon_{n2}^{(r)} \quad \cdots \quad \varepsilon_{nm_n}^{(r)}\right]$.

The next step is estimate the parameters of the multiresponse multipredictor semiparametric regression (MMSR) model on longitudinal data based on the truncated spline estimator by using the weighted least square (WLS) method that is by minimizing the number of weighted squared error. For this objective, we consider the following equation:

(7) $$L = \underset{\sim}{\varepsilon}^T \mathbf{V}^{-1} \underset{\sim}{\varepsilon} = \left(\underset{\sim}{y}^T \mathbf{V}^{-1} \underset{\sim}{y}\right) - 2\left(\underset{\sim}{y}^T \mathbf{V}^{-1}\left(\mathbf{X}\underset{\sim}{\beta}\right)\right) - 2\left(\underset{\sim}{y}^T \mathbf{V}^{-1}\left(\mathbf{Z}\underset{\sim}{\alpha}\right)\right) - \left(\underset{\sim}{y}^T \mathbf{V}^{-1}\left(\mathbf{Z}\underset{\sim}{\alpha}\right)\right) + \left(\left(\mathbf{X}\underset{\sim}{\beta}\right)^T \mathbf{V}^{-1}\left(\mathbf{X}\underset{\sim}{\beta}\right)\right) + 2\left(\left(\mathbf{X}\underset{\sim}{\beta}\right)^T \mathbf{V}^{-1}\left(\mathbf{Z}\underset{\sim}{\alpha}\right)\right) + \left(\left(\mathbf{Z}\underset{\sim}{\alpha}\right)^T \mathbf{V}^{-1}\left(\mathbf{Z}\underset{\sim}{\alpha}\right)\right)$$

To estimate the model parameters, the partial derivative of (7) with respect to parameters $\underset{\sim}{\beta}$ and $\underset{\sim}{\alpha}$ is equaled to zero. Hence we have:

$\frac{\partial L}{\partial \beta} = \underset{\sim}{0}$ and the result is as follows:

(8) $$\frac{\partial L}{\partial \beta} = \left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\left(\underset{\sim}{y} - \mathbf{Z}\underset{\sim}{\alpha}\right) = \underset{\sim}{0}$$

(9) $$\frac{\partial L}{\partial \alpha} = \left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\left(\underset{\sim}{y} - \left(\mathbf{X}\underset{\sim}{\beta}\right)\right) = \underset{\sim}{0}$$

Next, based on equations (8) and (9), we obtain the estimations of parameters $\underset{\sim}{\beta}$ and $\underset{\sim}{\alpha}$ as follows:

(10) $$\hat{\underset{\sim}{\beta}} = \left[\mathbf{I} - \left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{X}\right]^{-1}\left(\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1} - \left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\right)\underset{\sim}{y}$$

(11) $$\hat{\underset{\sim}{\alpha}} = \left[\mathbf{I} - \left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{X}\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\right]^{-1}\left(\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1} - \left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{X}\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\right)\underset{\sim}{y}$$

Furthermore, the equations (10) and (11) can be rewritten as follows:

(12) $$\hat{\underset{\sim}{\beta}} = B\underset{\sim}{y}$$

(13) $$\hat{\underset{\sim}{\alpha}} = A\underset{\sim}{y}$$

where:

(14) $$B = \left[\mathbf{I} - \left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{X}\right]^{-1} \times$$
$$\left(\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\right) - \left(\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\right)$$

(15) $$A = \left[\mathbf{I} - \left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\mathbf{Z}\right]^{-1}\left(\left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1} - \left(\mathbf{Z}^T\mathbf{V}^{-1}\mathbf{Z}\right)^{-1}\mathbf{Z}^T\mathbf{V}^{-1}\left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\right)$$

Next, we determine the distribution of $\underset{\sim}{y}$. Since $\underset{\sim}{y}$ is a linear combination of $\underset{\sim}{\varepsilon}$ then $\underset{\sim}{y}$ follows the normal distribution that is $\underset{\sim}{y} \sim \left(E\left(\underset{\sim}{y}\right), Var\left(\underset{\sim}{y}\right)\right)$ where:

(16) $$E(\underset{\sim}{y}) = \left(\mathbf{X}B + \mathbf{Z}A\right)\underset{\sim}{y} = C\underset{\sim}{y}$$

for $C = \mathbf{X}B + \mathbf{Z}A$, and

(17) $$Var(\underset{\sim}{y}) = \mathbf{V}$$

Then we determine the distribution of parameters $\hat{\underset{\sim}{\beta}}$ and $\hat{\underset{\sim}{\alpha}}$ by taking the means and variances as follows:

(18) $E\left(\hat{\underset{\sim}{\beta}}\right) = B\,C\underset{\sim}{y}$

(19) $Var\left(\hat{\underset{\sim}{\beta}}\right) = B\,\mathbf{V}B^T$

(20) $E\left(\hat{\underset{\sim}{\alpha}}\right) = AC\underset{\sim}{y}$

(21) $Var\left(\hat{\underset{\sim}{\alpha}}\right) = A\mathbf{V}A^T$

In the following section, we discuss the determining the shortest $(1-\alpha)100\%$ confidence interval for parameters $\hat{\underset{\sim}{\beta}}$ and $\hat{\underset{\sim}{\alpha}}$ by taking the pivotal quantity $\hat{\underset{\sim}{\beta}}$ and $\hat{\underset{\sim}{\alpha}}$.

3.1. The Confidence Interval of Parameter $\hat{\underset{\sim}{\beta}}$

The shortest $(1-\alpha)100\%$ confidence interval for $\left(\hat{\underset{\sim}{\beta}}\right)_h$, $h = 1,2,\ldots,R(1+a)$ can be done by determining the Pivotal quantity for the parameter $\hat{\underset{\sim}{\beta}}$. Pivotal quantity $U_h(x_1, x_2, \ldots, x_a)$ by doing the following transformation:

(22) $$U_h(x_1, x_2, \ldots, x_a) = \frac{\left(\underset{\sim}{\beta}\right)_h - E\left(\hat{\underset{\sim}{\beta}}\right)_h}{\sqrt{Var\left(\hat{\underset{\sim}{\beta}}\right)_h}} = \frac{\left(\underset{\sim}{\beta}\right)_h - \left(\hat{\underset{\sim}{\beta}}\right)_h}{\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}}$$

Furthermore, it can be shown that U_h has a standard normal distribution with a mean of 0 and a variance of 1, $U_h \sim N(0,1)$ as follows:

(23) $$\begin{aligned} E\left(U_h\right) &= E\left(\frac{\left(\underset{\sim}{\beta}\right)_h - \left(\hat{\underset{\sim}{\beta}}\right)_h}{\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}}\right) = \frac{1}{\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}}\left(E\left(\underset{\sim}{\beta}\right)_h - E\left(\hat{\underset{\sim}{\beta}}\right)_h\right) \\ &= \frac{1}{\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}}\left(\left(\hat{\underset{\sim}{\beta}}\right)_h - \left(\hat{\underset{\sim}{\beta}}\right)_h\right) = 0 \end{aligned}$$

(24) $$\begin{aligned} \mathrm{Var}\left(U_h\right) &= \mathrm{Var}\left(\frac{\left(\underset{\sim}{\beta}\right)_h - \left(\hat{\underset{\sim}{\beta}}\right)_h}{\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}}\right) = \frac{1}{\left(\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}\right)^2}\left(\mathrm{Var}\left(\underset{\sim}{\beta}\right)_h - \mathrm{Var}\left(\hat{\underset{\sim}{\beta}}\right)_h\right) \\ &= \frac{1}{\left(B\mathbf{V}B^T\right)_{hh}}\left(B\mathbf{V}B^T\right)_{hh} = 1 \end{aligned}$$

Based on equations (23) and (24), it can be proved that the distribution of $U_h \sim N(0,1)$, in other words U_h has a standard normal distribution (Z). So U_h is the pivotal quantity for $(\underset{\sim}{\beta})_h$, where $(\underset{\sim}{\beta})_h$ is the *h*-th element of the $\underset{\sim}{\beta}$ vector, while *hh* is the *h*-diagonal element of the $(B\mathbf{V}B^T)$ matrix. Then determine the confidence interval $(1-\alpha)100\%$ by solving the probability of equation (22) is as follows:

(25) $$P(a_h \leq U_h(x_1,x_2,...,x_a) \leq b_h) = 1-\alpha$$

where a_h is the lower limit of the interval; b_h is the upper limit of the interval; and

$(1-\alpha)$ = level of confidence.

If equation (22) is substituted into equation (25), then the following equation will be obtained:

(26) $$P\left(a_h \leq \frac{(\underset{\sim}{\beta})_h - (\hat{\underset{\sim}{\beta}})_h}{\sqrt{(B\mathbf{V}B^T)_{hh}}} \leq b_h \right) = 1-\alpha$$

Next, we determine the values of $a_h \in R$ and $b_h \in R$. At this step, the shortest $(1-\alpha)100\%$ confidence interval can be written as follows:

(27) $$\begin{aligned} L(a_h,b_h) &= \left((\hat{\underset{\sim}{\beta}})_h - b_h\sqrt{(B\mathbf{V}B^T)_{hh}} \leq (\underset{\sim}{\beta})_h \leq (\hat{\underset{\sim}{\beta}})_h - a_h\sqrt{(B\mathbf{V}B^T)_{hh}} \right) \\ &= (b_h - a_h)\sqrt{(B\mathbf{V}B^T)_{hh}} \end{aligned}$$

To obtain the shortest $(1-\alpha)100\%$ confidence interval, we taking the solution to the conditional optimization as follows:

(28) $$\underset{a_h,b_h \in R}{\text{Min}}\left\{L(a_h,b_h)\right\} = \underset{a_h,b_h \in R}{\text{Min}}\left\{(b_h,a_h)\sqrt{(B\mathbf{V}B^T)_{hh}}\right\}$$

with the provision of:

(29) $$\int_{a_h}^{b_h} \rho(m_h)\,dm_h = 1-\alpha \quad \text{atau} \quad \varphi(b_v) - \varphi(a_v) = 1-\alpha$$

where ρ the distribution of *Z* and φ is the cumulative probability distribution of *Z*. Next, we perform optimization by forming the Lagrange function as follows:

(30) $$G(a_h,b_h,\lambda)=(b_h-a_h)\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}+\lambda\left(\varphi(b_h)-\varphi(a_h)-(1-\alpha)\right)$$

where λ is a Lagrange constant. Then, the partial derivative of the function given by equation (30) is performed for each a_h,b_h,λ.

(31) $$\frac{\partial G(a_h,b_h,\lambda)}{\partial a_h}=-\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}-\lambda\varphi(a_h)=0$$

(32) $$\frac{\partial G(a_h,b_h,\lambda)}{\partial b_h}=\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}+\lambda\varphi(b_h)=0$$

(33) $$\frac{\partial G(a_h,b_h,\lambda)}{\lambda}=\varphi(b_h)-\varphi(a_h)-(1-\alpha)=0$$

Hence, the results obtained based on equations (31) and (32) are as follows:

(34) $$\begin{array}{r} -\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}-\lambda\varphi(a_h)=0 \\ \sqrt{\left(B\mathbf{V}B^T\right)_{hh}}+\lambda\varphi(b_h)=0 \\ \hline \lambda\left(\varphi(b_h)-\varphi(a_h)\right)\ =0 \\ \rho(b_h)=\rho(a_h) \end{array}+$$

From equation (29), the probability of b_h and a_h is the same, meaning that in the standard normal distribution the value of b_h and a_h is the opposite. So, the shortest $(1-\alpha)100\%$ confidence interval must be taken the value of $b_h=-a_h$ which fulfills the following equation:

(35) $$\int_{-\infty}^{-a_h}\rho(m_h)dm=\int_{b_h}^{\infty}\rho(m_h)dm=\frac{\alpha}{2}$$

where $-a_h=-Z_{\frac{\alpha}{2}}$ and $b_h=Z_{\frac{\alpha}{2}}$.

The value of a_h and b_h can be seen in the standard normal distribution (Z) table. So, the shortest $(1-\alpha)100\%$ confidence interval for the parameter $\underset{\sim}{\beta}$ of the multiresponse multipredictor semiparametric regression (MMSR) model on longitudinal data based on a truncated spline estimator is as follows:

(36) $$P\left(\left(\hat{\underset{\sim}{\beta}}\right)_h - a_h\sqrt{\left(B\mathbf{V}B^T\right)_{hh}} < \left(\underset{\sim}{\beta}\right)_h < \left(\hat{\underset{\sim}{\beta}}\right)_h + b_h\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}\right) = 1-\alpha$$

From equation (36) and by using the standard normal distribution, the following confidence intervals are obtained:

(37) $$P\left(\left(\hat{\underset{\sim}{\beta}}\right)_h - Z_{\frac{\alpha}{2}}\sqrt{\left(B\mathbf{V}B^T\right)_{hh}} < \left(\underset{\sim}{\beta}\right)_h < \left(\hat{\underset{\sim}{\beta}}\right)_h + Z_{\frac{\alpha}{2}}\sqrt{\left(B\mathbf{V}B^T\right)_{hh}}\right) = 1-\alpha$$

3.2. The Confidence Interval of Parameter $\hat{\underset{\sim}{\alpha}}$

The shortest $(1-\alpha)100\%$ confidence interval of $\left(\hat{\underset{\sim}{\alpha}}\right)_k$ for $k = 1, 2, \ldots, \left(R + \sum_{i=1}^{R}\sum_{q=1}^{b} D_q^{(r)} + K_q^{(r)}\right)$ can be done by specifying the pivotal quantity for the parameter $\hat{\underset{\sim}{\alpha}}$. Pivotal quantity $U_k(t_1, t_2, \ldots, t_b)$ is obtained by performing the following transformation:

(38) $$U_k(t_1, t_2, \ldots, t_b) = \frac{(\underset{\sim}{\alpha})_k - E(\hat{\underset{\sim}{\alpha}})_k}{\sqrt{Var(\hat{\underset{\sim}{\alpha}})_k}} = \frac{(\underset{\sim}{\alpha})_k - (\hat{\underset{\sim}{\alpha}})_k}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}}$$

Furthermore, it can be shown that U_k has a standard normal distribution with a mean of zero and a variance of one, namely $U_k \sim N(0,1)$ as follows:

(39) $$\begin{aligned} E\left(U_k\right) &= E\left(\frac{(\underset{\sim}{\alpha})_k - (\hat{\underset{\sim}{\alpha}})_k}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}}\right) = \frac{1}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}}\left(E\left(\underset{\sim}{\alpha}\right)_k - E\left(\hat{\underset{\sim}{\alpha}}\right)_k\right) \\ &= \frac{1}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}}\left((\hat{\underset{\sim}{\alpha}})_k - (\hat{\underset{\sim}{\alpha}})_k\right) = 0 \end{aligned}$$

(40) $$\begin{aligned} \mathrm{Var}\left(U_k\right) &= \mathrm{Var}\left(\frac{(\underset{\sim}{\alpha})_k - (\hat{\underset{\sim}{\alpha}})_k}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}}\right) = \frac{1}{\left(\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}\right)^2}\left(\mathrm{Var}\left(\underset{\sim}{\alpha}\right)_k - \mathrm{Var}\left(\hat{\underset{\sim}{\alpha}}\right)_k\right) \\ &= \frac{1}{\left(A\mathbf{V}A^T\right)_{kk}}\left(A\mathbf{V}A^T\right)_{kk} = 1 \end{aligned}$$

From equations (39) and (40), it can be proved that $U_k \sim N\left(0,1\right)$, in other words U_k has a standard normal distribution (Z). So, U_k is the pivotal quantity for $\left(\underset{\sim}{\alpha}\right)_k$, where $\left(\underset{\sim}{\alpha}\right)_k$ is the *k*-th element of the vector $\underset{\sim}{\alpha}$, while kk is the k-th diagonal element of the matrix $\left(A\mathbf{V}A^T\right)$. Next, we determine the $(1-\alpha)100\%$ confidence interval by solving the probability of equation (38) as follows:

(41) $$P\left(a_k \le U_k(t_1,t_2,...,t_b) \le b_k\right) = 1-\alpha$$

where a_k is the lower limit of the interval; b_k is the upper limit of the interval; and $(1-\alpha)$ = level of confidence.

Furthermore, if equation (38) is substituted into equation (41), then the following equation will be obtained:

(42) $$P\left(a_k \le \frac{(\hat{\underset{\sim}{\alpha}})_k - (\underset{\sim}{\alpha})_k}{\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}} \le b_k\right) = 1-\alpha$$

Then we determine the value of $a_k \in R$ dan $b_k \in R$. So, the shortest $(1-\alpha)100\%$ confidence interval can be written as follows:

(43) $$\begin{aligned} L(a_k,b_k) &= \left((\hat{\underset{\sim}{\alpha}})_k - b_k\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} \le (\underset{\sim}{\alpha})_k \le (\hat{\underset{\sim}{\alpha}})_k + a_k\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}\right) \\ &= (b_k - a_k)\sqrt{\left(B\mathbf{V}B^T\right)_{kk}} \end{aligned}$$

The shortest $(1-\alpha)100\%$ confidence interval is obtained by solving the conditional optimization as follows:

(44) $$\underset{a_k,b_k\in R}{\text{Min}}\left\{L(a_k,b_k)\right\} = \underset{a_k,b_k\in R}{\text{Min}}\left\{(b_k,a_k)\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}\right\}$$

with the provision of:

(45) $$\int_{a_k}^{b_k} \rho(m_k)\,dm_k = 1-\alpha \quad \text{atau} \quad \varphi(b_v) - \varphi(a_v) = 1-\alpha$$

where ρ is distribution of Z and φ is the cumulative probability distribution of Z. Then, we perform optimization by forming the Lagrange function as follows:

(46) $$G(a_k,b_k,\lambda) = (b_k - a_k)\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} + \lambda\left(\varphi(b_k) - \varphi(a_k) - (1-\alpha)\right)$$

where λ is Lagrange's constant. Then the partial derivative of the function in equation (46) is performed on each a_k, b_k, λ as follows:

(47) $$\frac{\partial G(a_k, b_k, \lambda)}{\partial a_k} = -\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} - \lambda\varphi(a_k) = 0$$

(48) $$\frac{\partial G(a_k, b_k, \lambda)}{\partial b_k} = \sqrt{\left(A\mathbf{V}A^T\right)_{kk}} + \lambda\varphi(b_k) = 0$$

(49) $$\frac{\partial G(a_k, b_k, \lambda)}{\lambda} = \varphi(b_k) - \varphi(a_k) - (1-\alpha) = 0$$

Hence, the sum of the results of equations (47) and (48) is obtained as follows:

(50) $$\begin{array}{rl} -\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} - \lambda\varphi(a_k) = 0 & \\ \sqrt{\left(A\mathbf{V}A^T\right)_{kk}} + \lambda\varphi(b_k) = 0 & \\ \hline \lambda\left(\varphi(b_k) - \varphi(a_k)\right) \ = 0 & + \\ \rho(b_k) = \rho(a_k) & \end{array}$$

Next, based on equation (45), the probability of b_k and a_k are the same, meaning that in the standard normal distribution the values of b_k and a_k are the opposite. So, the shortest $(1-\alpha)100\%$ confidence interval must be taken the value of $b_k = -a_k$ which fulfills the following equation:

(51) $$\int_{-\infty}^{-a_k} \rho(m_k)\,dm = \int_{b_k}^{\infty} \rho(m_k)\,dm = \frac{\alpha}{2}$$

where $-a_k = -Z_{\frac{\alpha}{2}}$ and $b_k = Z_{\frac{\alpha}{2}}$. The value of a_k and b_k can be seen in the standard normal distribution table Z.

Hence, the shortest $(1-\alpha)100\%$ confidence interval of the parameter $\underset{\sim}{\alpha}$ of the multiresponse multipredictor semiparametric regression (MMSR) model on longitudinal data based on truncated spline estimator is as follows:

(52) $$P\left(\left(\hat{\underset{\sim}{\alpha}}\right)_k - a_k\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} < \left(\underset{\sim}{\alpha}\right)_k < \left(\hat{\underset{\sim}{\alpha}}\right)_k + b_k\sqrt{\left(A\mathbf{V}A^T\right)_{kk}}\right) = 1-\alpha \ .$$

From equation (52) and by using the standard normal distribution, the following $(1-\alpha)100\%$ confidence intervals are obtained:

(53) $$P\left((\hat{\underset{\sim}{\alpha}})_k - Z_{\frac{\alpha}{2}}\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} < (\underset{\sim}{\alpha})_h < (\hat{\underset{\sim}{\alpha}})_k + Z_{\frac{\alpha}{2}}\sqrt{\left(A\mathbf{V}A^T\right)_{kk}} \right) = 1-\alpha \quad .$$

4. CONCLUSIONS

Theoretically, based on equations (37) and (53) we can get the $(1-\alpha)100\%$ confidence interval for parameters in the MMSR model. Therefore, in the future, it can be used to model data of the Case Growth Rate (CGR) and Case Fatality Rate (CFR) COVID-19 in Indonesia, so that we can also determine what predictor variables significantly affect the Case Growth Rate (CGR) and Case Fatality Rate (CFR) COVID-19 in Indonesia.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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