

# Statistical Inference in a Growth Curve Quantile Regression Model for Longitudinal Data

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**SUMMARY.** This article describes a polynomial growth curve quantile regression model that provides a comprehensive assessment about the treatment effects on the changes of the distribution of outcomes over time. The proposed model has the flexibility, as it allows the degree of a polynomial to vary across quantiles. A high degree polynomial model fits the data adequately, yet it is not desirable due to the complexity of the model. We propose the model selection criterion based on an empirical loglikelihood that consistently identifies the optimal degree of a polynomial at each quantile. After the parsimonious model is fitted to the data, the hypothesis test is further developed to evaluate the treatment effects by comparing the growth curves. It is shown that the proposed empirical loglikelihood ratio test statistic follows a chi-square distribution asymptotically under the null hypothesis. Various simulation studies confirm that the proposed test successfully detects the difference between the curves across quantiles. When the empirical loglikelihood is employed, we incorporate the within-subject correlation commonly existing in longitudinal data and gain estimation efficiency of the quantile regression parameters in the growth curve model. The proposed process is illustrated through the analysis of randomized controlled longitudinal depression data.

**KEY WORDS:** Empirical loglikelihood; Hypothesis test; Model selection; Polynomial regression; Quantile regression.

## 1. Introduction

In longitudinal studies where subjects are repeatedly measured, it is of particular interest to analyze the growth of observations over time. For example, in a randomized controlled trial study conducted in Washington, D.C. from March 1997 through May 2002, women suffering from depression were randomly assigned to one of three treatments: an antidepressant medication, psychotherapy, or referral to community mental health services. The Hamilton depression rating scale was recorded monthly to evaluate effects of the different treatments on depression longitudinally. Although a growth curve mean regression model can provide the dynamic changes of depression scores over time (Potthoff and Roy, 1964), it could be problematic due to the following reasons. First, the distribution of depression scores at the initial visit is right-skewed as shown in Figure 1. Second, the treatment effects on the changes of the distribution of depression scores over time may vary across quantiles.

Growth curve quantile analysis is a viable alternative that provides a unique opportunity in exploring various trajectories of observations across levels of depression from mild to severe over time. Suppose that a polynomial growth curve with a sufficiently high degree is guaranteed to provide an arbitrarily good fit to the longitudinal data. We propose to model the  $\tau$ th growth curve quantiles of  $n_i$  responses from subject  $i$ ,  $\mathbf{Y}_i = (Y_{i1}, \dots, Y_{in_i})^T$ , repeatedly measured at times  $\mathbf{t}_i = (t_{i1}, \dots, t_{in_i})^T$  as

$$Q_\tau(\mathbf{Y}_i | \mathbf{T}_{\tau i}, \mathbf{H}_i) = \mathbf{T}_{\tau i} \mathbf{B}_\tau \mathbf{H}_i, \quad i = 1, \dots, n, \quad (1)$$

where  $\tau \in (0, 1)$ ,  $n$  is the number of subjects, and  $\mathbf{B}_\tau = (\mathbf{B}_{\tau 1}, \dots, \mathbf{B}_{\tau q})$  is a  $p_\tau \times q$ -dimensional matrix of

parameters. Note that the  $n_i \times p_\tau$ -dimensional matrix  $\mathbf{T}_i = (\mathbf{1}, \mathbf{t}_i, \dots, \mathbf{t}_i^{p_\tau-1})$  specifies a polynomial curve with a degree of  $p_\tau - 1$  and the  $q$ -dimensional treatment vector  $\mathbf{H}_i$  models differences between  $q$  treatment groups. In the aforementioned depression study, for instance, three treatment effects can be evaluated by comparing columns,  $\mathbf{B}_{\tau 1}$ ,  $\mathbf{B}_{\tau 2}$ , and  $\mathbf{B}_{\tau 3}$ , in the parameter matrix of  $\mathbf{B}_\tau$ . If diverse effects of the  $k$ th treatment on the response at different levels of  $\tau$  are of interest, we can assess  $\mathbf{B}_{\tau k}$  across quantiles. Therefore, we address statistical inference about the quantile regression parameters in model (1).

When polynomial growth curves are modeled, the selection of a proper degree of a polynomial plays an important role in achieving the most parsimonious growth curve model. We propose the Bayesian information criterion based on an empirical loglikelihood (Qin and Lawless, 1994; Owen, 2001) for the quantile regression model selection. This allows us to choose a different degree of a polynomial across quantiles. In theory, we show that the proposed criterion consistently identifies the optimal degree of a polynomial at a given level of  $\tau$ . After the parsimonious growth curve model is selected at the  $\tau$ th quantile of interest, one often evaluates the treatment effects by comparing the growth curves. We construct the hypothesis test to check if the pattern of the  $\tau$ th growth curve quantile differs reliably between groups. Typical loglikelihood ratio tests confront challenges for this hypothesis test because specification of a parametric likelihood function is unattainable in quantile regression models. In this article, we develop a simple and powerful test statistic based on an empirical loglikelihood ratio that is similar to the parametric loglikelihood ratio. This test statistic is easy to implement, since it does not require specification of the parametric likelihood

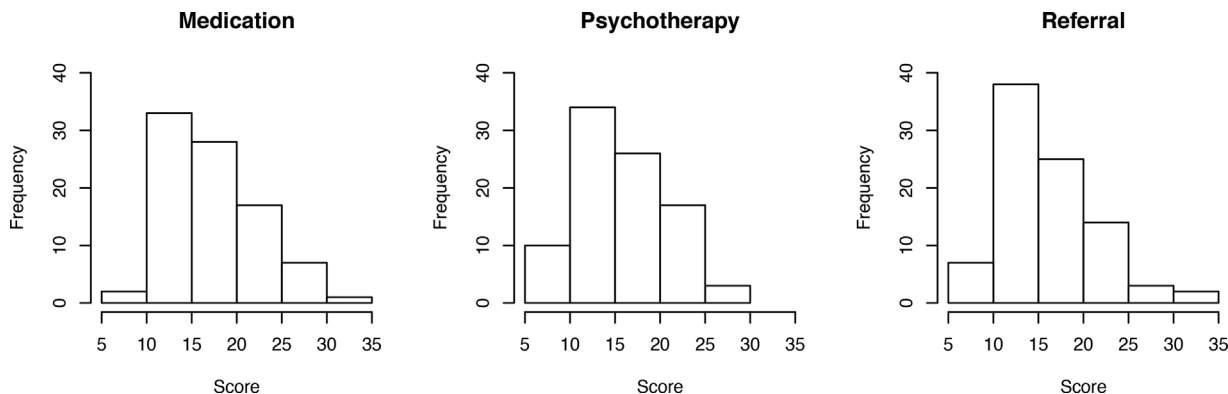


Figure 1. Histograms of depression scores at baseline for medication, psychotherapy, and referral group.

function, nor does it estimate a covariance matrix of estimates of the quantile regression parameters. We show that the proposed test statistic asymptotically follows a chi-square distribution under the null hypothesis. In addition, simulation studies demonstrate that the proposed test detects the difference between the growth curves successfully in all cases under consideration.

In longitudinal studies, measurements within the same subject are more likely to be correlated, and therefore estimation efficiency can be achieved by accounting for the within-subject correlation. This brings the challenge of incorporating the correlation information, as estimating the working correlation structure can be unreliable in quantile regression model (1) when either low or high quantile is of interest, or the number of measurements is relatively large. To attenuate this difficulty, we employ an empirical likelihood for longitudinal data (Cho, Hong, and Kim, 2016) by transforming model (1) to a standard quantile regression model. This method does not estimate the nuisance parameters associated with the working correlation structure, but approximates its inverse with several known basis matrices (Qu, Lindsay, and Li, 2000). Both theoretical and simulation results ensure that this estimation approach yields a more efficient estimator than the one assuming an independent correlation structure (Koenker and Bassett, 1978). Tang and Leng (2011) also used the empirical likelihood to improve estimation efficiency. However, their estimation approach is not applicable for the aforementioned model selection and hypothesis test, because the empirical likelihood is constructed under the mean regression framework, and there is appropriate for statistical inference about mean regression parameters, not quantile regression parameters of our interest.

The remainder of this article proceeds as follows: Section 2 provides efficient estimation for the regression quantiles in model (1), inference about testing for equality of growth curves, and selection of the most parsimonious growth curve model. In Section 3.1, we evaluate the finite sample performance of the proposed procedure through simulation studies. The proposed procedure is also applied to the aforementioned depression data in Section 3.2. In the analysis of the depression study, the proposed growth curve quantile model provides a more complete assessment about the treatment effects on the distribution of depression scores. A discussion is placed in Sections 4.

## 2. Methodology

### 2.1. Estimation of Quantile Regression Parameters

In this section, we consider efficient estimation of the quantile regression parameter  $\mathbf{B}_\tau$  in model (1). By letting  $\mathbf{X}_i = \mathbf{H}_i^T \otimes \mathbf{T}_{\tau i}$  and  $\boldsymbol{\beta} = (\mathbf{B}_{\tau 1}^T, \dots, \mathbf{B}_{\tau q}^T)^T$ , model (1) can be transformed to  $Q_\tau(\mathbf{Y}_i | \mathbf{X}_i) = \mathbf{X}_i \boldsymbol{\beta}$ , where  $\otimes$  is a left Kronecker product. To account for the within-subject correlation, we extend the generalized estimating equations (Liang and Zeger, 1986) and assess  $\boldsymbol{\beta}$  at a given level of  $\tau$  by solving

$$\sum_{i=1}^n \mathbf{X}_i^T \mathbf{A}_i^{-1/2} \mathbf{R}_i(\boldsymbol{\alpha})^{-1} \mathbf{A}_i^{-1/2} \varphi_\tau(\mathbf{Y}_i - \mathbf{X}_i \boldsymbol{\beta}) = 0, \quad (2)$$

where  $\mathbf{A}_i$  and  $\mathbf{R}_i(\boldsymbol{\alpha})$  are a diagonal variance matrix and a working correlation matrix of  $\varphi_\tau(\mathbf{Y}_i - \mathbf{X}_i \boldsymbol{\beta}_\tau)$  with a few nuisance parameters  $\boldsymbol{\alpha}$ ,  $\boldsymbol{\beta}_\tau$  is the true value of  $\boldsymbol{\beta}$  at the  $\tau$ th quantile level, and  $\varphi_\tau(u)$  is a first derivative of a check function  $\rho_\tau(u) = u\{\tau - 1(u < 0)\}$  having an indicator function  $1(\cdot)$ . This procedure enables us to improve estimation efficiency by incorporating the correlation among measurements within the subject, yet it requires estimation of  $\boldsymbol{\alpha}$  in the working correlation matrix. When the misspecified working correlation structure is considered, it may cause a loss of estimation efficiency. More importantly, this approach may not be generally applicable if low or high quantiles are of interest because estimation of  $\boldsymbol{\alpha}$  can be unreliable. Even if  $\boldsymbol{\beta}$  is estimated by solving equation (2), this estimator may satisfy the equations approximately due to the discontinuity of  $\varphi_\tau(\mathbf{Y}_i - \mathbf{X}_i \boldsymbol{\beta})$ .

Alternatively, Qu, Lindsay, and Li (2000) modeled the inverse of the working correlation matrix in (2) as  $\mathbf{R}_i(\boldsymbol{\alpha})^{-1} = \sum_{j=1}^b d_j \mathbf{D}_{ij}$ , where  $\mathbf{D}_{i1}$  is the identity matrix,  $\mathbf{D}_{i2}, \dots, \mathbf{D}_{ib}$  are symmetric matrices that contain either 0 or 1 as components, and  $d_1, \dots, d_b$  are unknown constants. In practice, the set of basis matrices can be readily determined by the type of working correlation structures. For example, when the measurement times are spaced evenly and the measurements are less likely to be correlated if they are further away in time, as in our real data, the AR(1) is generally considered as the working correlation structure. As a result, the inverse of the working correlation structure is approximated by a linear combination of three basis matrices,  $\mathbf{D}_{i1}$ ,  $\mathbf{D}_{i2}$ , and  $\mathbf{D}_{i3}$ , where  $\mathbf{D}_{i2}$  is a symmetric matrix with 1 on the sub-diagonal and 0 elsewhere and  $\mathbf{D}_{i3}$  is a symmetric matrix with 1 in elements

(1, 1) and  $(n_i, n_i)$  and 0 elsewhere. If the correlations among all measurements within each subject are likely to be equal, then  $\mathbf{R}_i(\boldsymbol{\alpha})$  corresponds to a compound symmetry structure and only two basis matrices are needed to represent  $\mathbf{R}_i(\boldsymbol{\alpha})^{-1}$  as  $\mathbf{R}_i(\boldsymbol{\alpha})^{-1} = d_1 \mathbf{D}_{i1} + d_2 \mathbf{D}_{i2}$ , where  $\mathbf{D}_{i2}$  is a symmetric matrix with 0 on the diagonal and 1 elsewhere, and  $d_1$  and  $d_2$  are unknown coefficients. If the prior information for correlation structure is not known, one can use a linear representation of a complete set of basis matrices with 1 for  $(i, j)$  and  $(j, i)$  entries and 0 elsewhere. Further details about the choice of the basis matrices can be found in Qu, Lindsay, and Li (2000) and Zhou and Qu (2012).

With the basis matrices  $\mathbf{D}_{i1}, \dots, \mathbf{D}_{ib}$  and  $\text{var}\{\varphi_\tau(Y_{ij} - \mathbf{X}_{ij}\boldsymbol{\beta}_\tau)\} = \tau(1 - \tau)$  for all  $j$ , equation (2) can be extended as  $\sum_{i=1}^n \mathbf{g}_i(\boldsymbol{\beta}) = 0$  having

$$\mathbf{g}_i(\boldsymbol{\beta}) = \begin{pmatrix} \mathbf{X}_i^T \mathbf{D}_{i1} \varphi_\tau(\mathbf{Y}_i - \mathbf{X}_i \boldsymbol{\beta}) \\ \vdots \\ \mathbf{X}_i^T \mathbf{D}_{ib} \varphi_\tau(\mathbf{Y}_i - \mathbf{X}_i \boldsymbol{\beta}) \end{pmatrix}.$$

Following  $E\{\mathbf{g}_i(\boldsymbol{\beta}_\tau)\} = 0$ , we construct an empirical loglikelihood for estimation of growth curve quantile coefficients as

$$l_\tau(\boldsymbol{\beta}) = \sup \left\{ \sum_{i=1}^n \log(p_i) \mid \sum_{i=1}^n p_i \mathbf{g}_i(\boldsymbol{\beta}) = 0, \sum_{i=1}^n p_i = 1, 0 \leq p_i \leq 1 \right\}, \quad (3)$$

where  $p_i$  denotes a point mass assigned to subject  $i$ . The empirical loglikelihood estimator of  $\boldsymbol{\beta}$  is obtained by maximizing (3) as  $\hat{\boldsymbol{\beta}} = \arg \max_{\boldsymbol{\beta}} l_\tau(\boldsymbol{\beta})$ . In practice, the proposed approach is easy to be implemented by existing R packages. With an initial value of  $\boldsymbol{\beta}$ , the empirical loglikelihood (3) is computed by the R package `emplik`. The estimator is then implemented in the R package `optim` by maximizing the objective function of  $l_\tau(\boldsymbol{\beta})$ . Note that  $l_\tau(\boldsymbol{\beta})$  is not a convex function so it might cause the potential problem of multiple roots. Therefore, the choice of the initial value of  $\boldsymbol{\beta}$  plays an important role in achieving a consistent and efficient estimator. In the article, the R package `rq` is used to obtain the initial value, since this estimate is asymptotically consistent (Koenker and Bassett, 1978). Various simulation studies confirm that our resultant estimator is unbiased and more efficient than that obtained from Koenker and Bassett's method. We have provided R code used for Section 3.2 as Supplementary Materials.

Remark that the proposed approach takes into account the within-subject correlation without estimating additional nuisance parameters associated with the working correlation structure. Even when the assumed working correlation structure is specified incorrectly, the resultant estimator is still consistent. For statistical inference on quantile regression parameters, the empirical loglikelihood ratio is also formulated as

$$W_\tau(\boldsymbol{\beta}) = -2 \sum_{i=1}^n \log(np_i) = 2 \sum_{i=1}^n \log \{1 + \boldsymbol{\lambda}^T \mathbf{g}_i(\boldsymbol{\beta})\}, \quad (4)$$

where  $\boldsymbol{\lambda}$  satisfies  $n^{-1} \sum_{i=1}^n \mathbf{g}_i(\boldsymbol{\beta}) / \{1 + \boldsymbol{\lambda}^T \mathbf{g}_i(\boldsymbol{\beta})\} = 0$ . This function plays an inferential role since it possesses the

same chi-square asymptotic properties as in the parametric likelihood ratio test.

To study asymptotic properties of  $\hat{\boldsymbol{\beta}}$ , we denote the  $r$ th quantile of the conditional distribution of  $Y_{ij}$  given  $\mathbf{X}_{ij}$  by  $q_{ij}(\tau)$  and the conditional density at  $q_{ij}(\tau)$  given  $\mathbf{X}_{ij}$  by  $f_{ij}\{q_{ij}(\tau)\}$ , respectively. We also define  $\boldsymbol{\Delta}_i = \text{diag} [f_{i1}\{q_{i1}(\tau)\}/(\sqrt{\tau}\sqrt{1-\tau}), \dots, f_{in_i}\{q_{in_i}(\tau)\}/(\sqrt{\tau}\sqrt{1-\tau})]$ ,  $\boldsymbol{\Omega} = E\{\mathbf{g}_i(\boldsymbol{\beta}_\tau)\mathbf{g}_i(\boldsymbol{\beta}_\tau)^T\}$ , and  $\boldsymbol{\Gamma}^T = E(-\mathbf{X}_i^T \mathbf{D}_{i1} \boldsymbol{\Delta}_i \mathbf{X}_i, \dots, -\mathbf{X}_i^T \mathbf{D}_{ib} \boldsymbol{\Delta}_i \mathbf{X}_i)$ .

**THEOREM 1.** *Under the regularity conditions in the Supplementary Materials, the distribution of  $\sqrt{n}(\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}_\tau)$  converges to  $N\{\mathbf{0}, (\boldsymbol{\Gamma}^T \boldsymbol{\Omega}^{-1} \boldsymbol{\Gamma})^{-1}\}$  in distribution as  $n \rightarrow \infty$ . Moreover,  $\boldsymbol{\Sigma}_1 - \boldsymbol{\Sigma}$  is positive semidefinite, where  $\boldsymbol{\Sigma} = (\boldsymbol{\Gamma}^T \boldsymbol{\Omega}^{-1} \boldsymbol{\Gamma})^{-1}$  and  $\boldsymbol{\Sigma}_1$  is the asymptotic covariance matrix of  $\hat{\boldsymbol{\beta}}$  assuming an independent working correlation matrix.*

Theorem 1 confirms that the proposed estimator follows an asymptotic normal distribution regardless of the choice of working correlation structures. However, the positive semidefinite of  $\boldsymbol{\Sigma}_1 - \boldsymbol{\Sigma}$  ensures that estimation efficiency is improved when the within-subject correlation is accommodated. This efficiency gain can be achieved even though the working correlation structure is not specified correctly.

## 2.2. Hypothesis Test for Equality of Growth Curves

After we fit model (1) to the longitudinal data, one often asks whether or not the growth curves are identical at a level of  $\tau$ . For ease of presentation, we suppose that it is of particular interest to test the equality of the first  $d$  growth curves. Then, we construct the hypothesis test to check if these growth curves are the same at a given level of  $\tau$  by stating the null hypothesis as

$$H_0 : \mathbf{B}_{\tau 1} = \mathbf{B}_{\tau 2} = \dots = \mathbf{B}_{\tau d}. \quad (5)$$

As a special case, equality of all curves can be assessed by letting  $d = q$ . Since  $W_\tau(\boldsymbol{\beta})$  in equation (4) plays similarly to the parametric loglikelihood ratio, we develop the test statistic based on  $W_\tau(\boldsymbol{\beta})$  for testing the null hypothesis against the alternative that is the negation of  $H_0$  as

$$\text{ELT}_\tau = W_\tau(\tilde{\boldsymbol{\beta}}) - W_\tau(\hat{\boldsymbol{\beta}}), \quad (6)$$

where  $\tilde{\boldsymbol{\beta}}$  is the maximizer of  $l_\tau(\boldsymbol{\beta})$  under the null hypothesis. Note that  $W_\tau(\boldsymbol{\beta})$  and  $W_\tau(\tilde{\boldsymbol{\beta}})$  measure how well growth curve model (1) fits the data under the null and alternative hypotheses, respectively. The proposed test statistic is very beneficial, especially for quantile regression, since it does not require specification of parametric likelihood functions, nor does it estimate a covariance matrix associated with the quantile regression parameter.

**THEOREM 2.** *If the regularity conditions in the Supplementary Materials hold, then with a given level of  $\tau$ , the distribution of  $\text{ELT}_\tau$  converges to  $\chi_{p_\tau(d-1)}^2$  in distribution as  $n \rightarrow \infty$  under  $H_0$ .*

Theorem 2 confirms that the test statistic asymptotically follows a chi-square distribution with  $p_\tau(d-1)$  degrees of freedom when the null hypothesis is true. Thus, this proposed hypothesis test is easy to implement with the critical

value provided by the limiting distribution as  $\chi^2_{1-a, p_\tau(d-1)}$  at a significance level of  $a$ , where  $\chi^2_{1-a, p_\tau(d-1)}$  is the  $1 - a$  quantile of  $\chi^2_{p_\tau(d-1)}$ . In addition, the proposed test can be readily extended to find significant polynomials by setting coefficients of interesting polynomials as zero for the null hypothesis.

2.3. Selection of the Most Parsimonious Model

The choice of an optimal degree of a polynomial, denoted by  $p_\tau - 1$ , is essential for selecting the most suitable growth curve model at the  $\tau$ th quantile level in that  $p_\tau$  can vary with respect to  $\tau$ . In general, there may exist more than one correct model, since the most parsimonious model is usually nested within other growth curve models with a higher degree than  $p_\tau - 1$ . Although a cross validation and generalized cross validation can be commonly used for selecting a proper degree of a polynomial, these methods tend to overfit the model (Wang, Li, and Tsai, 2007). More importantly, these approaches may not be generally applicable for the quantile regression model directly.

Alternatively, the Bayesian information criterion based approach enables us to identify the most parsimonious correct model consistently. Suppose that the first  $m$  polynomial growth curves are candidate models holding  $p_\tau \leq m$  and index each candidate model by  $p$ , that is,  $p = 1, \dots, m$ . Given an arbitrary value of  $p$ , we denote  $\widehat{\mathbf{B}}(p) = (\widehat{\mathbf{B}}_1(p), \dots, \widehat{\mathbf{B}}_q(p)) = (\widehat{\mathbf{B}}^T, \mathbf{O}^T)^T$ , where  $\widehat{\mathbf{B}}$  is an  $p \times q$ -dimensional estimator matrix of  $\mathbf{B}$  in model (1) obtained by maximizing (3), and  $\mathbf{O}$  is an  $(m - p) \times q$ -dimensional matrix of zeros. With  $\widehat{\boldsymbol{\beta}}(p) = (\widehat{\mathbf{B}}_1(p)^T, \dots, \widehat{\mathbf{B}}_q(p)^T)^T$ , we propose the Bayesian

information criterion based on the empirical loglikelihood ratio as

$$ELBIC(p) = W_\tau(\widehat{\boldsymbol{\beta}}(p)) + df_p \log(n), \tag{7}$$

where  $df_p$  is the number of non-zero coefficients in  $\widehat{\boldsymbol{\beta}}(p)$ . The optimal degree of a polynomial is then obtained by minimizing (7) as  $\widehat{p} = \arg \min_p ELBIC(p)$ .

**THEOREM 3.** *Under the regularity conditions in the Supplementary Materials, with probability tending to 1,  $P(ELBIC(p) > ELBIC(p_\tau)) \rightarrow 1$  for all  $p \neq \widehat{p}$ .*

Theorem 3 ensures that the proposed criterion selects the most parsimonious growth curve model consistently. We also remark that the growth curve quantiles at the  $\tau$ th quantile level are constant over time when  $\widehat{p} = 1$ .

3. Numerical Studies

In this section, we evaluate the finite sample performance of the proposed procedure through simulation studies and a motivating example discussed in Section 1.

3.1. Simulation Studies

To reflect the real data example provided in Section 3.2, three growth curves are considered as follows. Each group consists of 100 subjects and every subject is repeatedly measured seven times at  $t = 0, 1, \dots, 6$ . Accordingly, the correlated response

Table 1

Standard errors of estimators obtained from the method by Koenker and Bassett (1978), Tang and Leng (2011), and the proposed approach

	$\rho = 0.3$			$\rho = 0.5$			$\rho = 0.8$		
	Proposed	K & B	T & L	Proposed	K & B	T & L	Proposed	K & B	T & L
$\tau = 0.25$									
$\beta_1$	0.071	0.076	0.072	0.070	0.080	0.072	0.070	0.084	0.075
$\beta_2$	0.039	0.042	0.039	0.041	0.044	0.042	0.048	0.050	0.045
$\beta_3$	0.070	0.076	0.069	0.069	0.078	0.071	0.070	0.088	0.076
$\beta_4$	0.040	0.041	0.041	0.042	0.044	0.042	0.045	0.048	0.045
$\beta_5$	0.066	0.073	0.068	0.066	0.076	0.067	0.070	0.086	0.075
$\beta_6$	0.040	0.042	0.040	0.040	0.043	0.041	0.049	0.048	0.049
$\tau = 0.50$									
$\beta_1$	0.064	0.069	0.063	0.065	0.075	0.066	0.066	0.079	0.065
$\beta_2$	0.038	0.039	0.038	0.040	0.042	0.040	0.043	0.045	0.041
$\beta_3$	0.062	0.067	0.063	0.065	0.074	0.066	0.069	0.082	0.069
$\beta_4$	0.036	0.038	0.037	0.039	0.040	0.038	0.040	0.041	0.038
$\beta_5$	0.064	0.068	0.065	0.062	0.073	0.062	0.065	0.076	0.067
$\beta_6$	0.036	0.036	0.035	0.041	0.042	0.040	0.042	0.042	0.043
$\tau = 0.75$									
$\beta_1$	0.070	0.073	0.071	0.072	0.081	0.073	0.071	0.083	0.073
$\beta_2$	0.039	0.041	0.040	0.042	0.044	0.042	0.045	0.045	0.043
$\beta_3$	0.066	0.070	0.065	0.071	0.080	0.072	0.073	0.087	0.077
$\beta_4$	0.040	0.042	0.040	0.041	0.044	0.042	0.043	0.045	0.042
$\beta_5$	0.067	0.073	0.067	0.071	0.080	0.070	0.070	0.080	0.070
$\beta_6$	0.038	0.040	0.038	0.043	0.046	0.044	0.046	0.048	0.047

variables are modeled as

$$\begin{aligned}
 \mathbf{Y} &= \begin{pmatrix} 1 & 1 & \dots & 1 \\ 0 & 1 & \dots & 6 \end{pmatrix}^T \begin{pmatrix} \beta_1 & \beta_3 & \beta_5 \\ \beta_2 & \beta_4 & \beta_6 \end{pmatrix} \begin{pmatrix} \mathbf{1}_{100} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{1}_{100} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{1}_{100} \end{pmatrix}^T \\
 &+ \boldsymbol{\epsilon} = \mathbf{TBH} + \boldsymbol{\epsilon}, \tag{8}
 \end{aligned}$$

where  $\boldsymbol{\beta} = (\beta_1, \beta_2, \dots, \beta_6)^T = (20, -3, 20, -2, 20, -1)^T$ ,  $\mathbf{1}_{100}$  is an 100-dimensional one vector, and  $\boldsymbol{\epsilon} = (\boldsymbol{\epsilon}_1, \dots, \boldsymbol{\epsilon}_{300})$  is a  $7 \times 300$ -dimensional matrix of random errors with  $\boldsymbol{\epsilon}_i = (\epsilon_{i1}, \dots, \epsilon_{i7})^T$ . We generate the heteroscedastic errors as  $\epsilon_{ij} = (\frac{1}{2} + \frac{i-1}{3}) \eta_{ij}$  for  $i = 1, \dots, 300$ , where  $\boldsymbol{\eta}_i = (\eta_{i1}, \dots, \eta_{i7})^T \sim N(\mathbf{0}, \boldsymbol{\Sigma})$ ,  $\boldsymbol{\Sigma}$  is an AR(1) structure with a correlation coefficient of  $\rho = 0.3, 0.5, \text{ and } 0.8$ , respectively. This leads us to have different true values of the regression quantile  $\mathbf{B}_\tau$  at  $\tau = 0.25, 0.5, \text{ and } 0.75$  as

$$\begin{aligned}
 \mathbf{B}_{0.25} &= \begin{pmatrix} 19.66 & 19.66 & 19.66 \\ -3.22 & -2.22 & -1.22 \end{pmatrix}, \quad \mathbf{B}_{0.5} = \mathbf{B}, \\
 \mathbf{B}_{0.75} &= \begin{pmatrix} 20.34 & 20.34 & 20.34 \\ -2.78 & -1.78 & -0.78 \end{pmatrix}.
 \end{aligned}$$

These regression quantiles are assessed using the proposed approach under an AR(1) correlation structure and also compared with the one under an independent correlation structure (Koenker and Bassett, 1978).

Based on 500 simulation runs, we evaluate the bias and the standard error of estimators for  $\tau = 0.25, 0.5, \text{ and } 0.75$ . Table 1 reports the estimated standard error of each estimated coefficient, yet the bias is not reported here because the bias is virtually zero for all estimators. The results in Table 1 confirm that the proposed approach outperforms Koenker and Bassett’s one in terms of smaller standard errors for all cases. More specifically, the proposed method yields more efficient estimators as the within-subject correlations become stronger. For statistical inference on the regression quantiles,

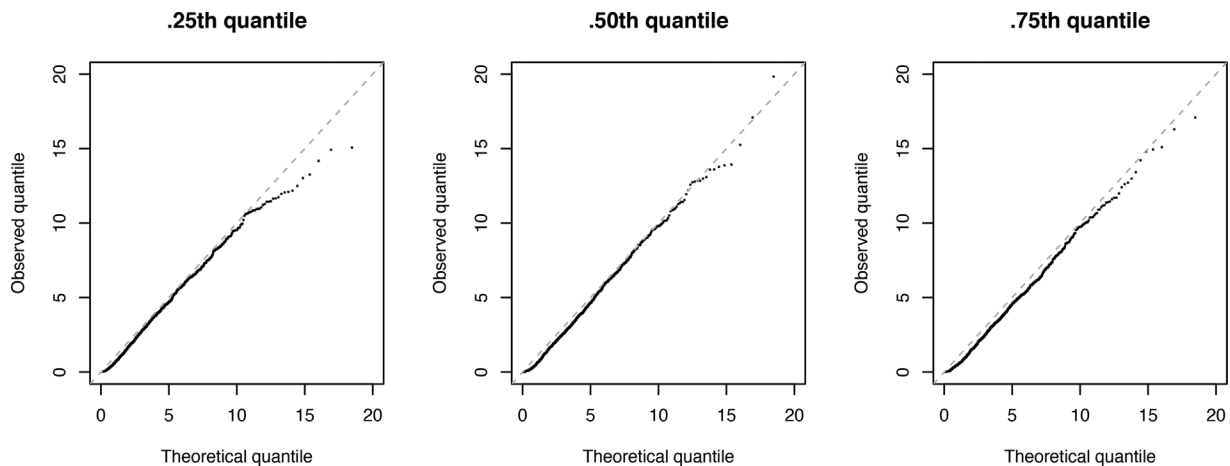
a coverage probability of a 95% bootstrap confidence interval is calculated using a sample standard error obtained from a bootstrapping approach in 500 bootstrap samples. Most of coverage probabilities are close to the nominal 95% level and are not reported. We also report the standard errors of estimators obtained by Tang and Leng’s approach under the AR(1) structure in Table 1. The results are comparable to those of the proposed estimators in cases under consideration.

For each simulated data set, all quantiles of the generated responses decrease linearly. As such, we evaluate whether or not the proposed criterion adopts the linear growth curve quantile as the most parsimonious model at three quantiles. The proportion of time that the ELBIC obtains  $\hat{p} \neq 2$  out of 500 simulations is less than 1% regardless of the level of the quantiles. This ensures that the proposed model selection approach chooses the true growth curve model with a high frequency. In addition, the proposed hypothesis test is conducted to assess the equality of the three growth curves. The proposed test detects the difference between the growth curves successfully, since the null hypothesis with  $d = 3$  in equation (5) is rejected every time at a significance level of 0.05 for all cases under consideration.

We further evaluate the finite sample performance of the proposed hypothesis test by generating three identical growth curves by setting  $\mathbf{B}$  in equation (8) as

$$\mathbf{B} = \begin{pmatrix} 20 & 20 & 20 \\ -1 & -1 & -1 \end{pmatrix}.$$

We compute test statistic (6) under the AR(1) structure and count the number of times  $H_0$  in (5) is rejected with  $d = 3$  at a significance level of 0.05 out of 500 simulations. The rejection rates (0.043, 0.049, and 0.046 at  $\tau = 0.25, 0.5, \text{ and } 0.75$ , respectively) are all close to the nominal level. In addition, three quantile–quantile plots reported in Figure 2 indicate that the empirical quantiles of the test statistic follow the theoretical chi-square quantiles sufficiently well under the null hypothesis.



**Figure 2.** Quantile–quantile plots for the chi-square distribution with four degrees of freedom versus the proposed test statistic testing the equality of the three curves at three quantiles.

3.2. Analysis of the Depression Study

We illustrate the proposed method through analysis of a randomized controlled trial study conducted in Washington, D.C. from March 1997 through May 2002. The data consist of 267 women who were suffering from depression. Participants were primarily working poor Latina and Black women who are less likely to receive appropriate treatment for depression care due to their minority status. They were randomly assigned to one of three groups: an antidepressant medication intervention (medication, 88 women), a psychotherapy intervention using manual-guided cognitive behavior therapy (psychotherapy, 90 women), or referral to community mental health services (referral, 89 women). The Hamilton depression rating scale was examined monthly from baseline through 6 months; women with higher scores indicate more severe depression. Further details about the design, methods and medical implications of the study can be found in Miranda et al. (2003).

The objective of this study is to explore the three treatment effects on different quantile levels of depression severity over time. Given the  $\tau$ th quantile level, the growth curve of depression scores for three groups is modeled as

$$Q_\tau(\mathbf{Y}|\mathbf{T}_\tau, \mathbf{H}) = \begin{pmatrix} 1 & 1 & \dots & 1 \\ 0 & 1 & \dots & 6 \\ \vdots & \vdots & \ddots & \vdots \\ 0^{p_\tau-1} & 1^{p_\tau-1} & \dots & 6^{p_\tau-1} \end{pmatrix}^T \begin{pmatrix} \beta_1 & \beta_{p_\tau+1} & \beta_{2p_\tau+1} \\ \vdots \\ \beta_{p_\tau} & \beta_{2p_\tau} & \beta_{3p_\tau} \end{pmatrix}$$

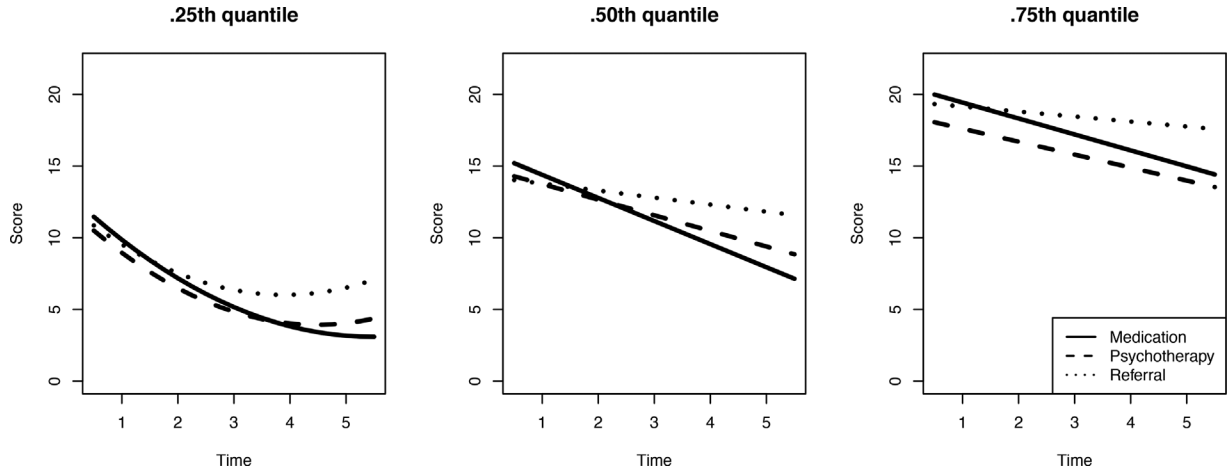
$$\times \begin{pmatrix} \mathbf{1}_{88} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{1}_{90} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{1}_{89} \end{pmatrix}^T = \mathbf{T}_\tau \mathbf{B}_\tau \mathbf{H}.$$

We evaluate the growth curve of the three treatments at  $\tau = 0.25, 0.5,$  and  $0.75$ . Before the model is assessed, we first select the most parsimonious model through the proposed criterion (7) under the AR(1) correlation structure at three levels of  $\tau$ , and adopt the quadratic growth curve for  $\tau = 0.25$ , and the linear growth curve for  $\tau = 0.5$  and  $0.75$ , respectively. Given the selected value of  $p_\tau$  at each  $\tau$ , we estimate  $\beta_i, i = 1, \dots, 3p_\tau$ , in  $\mathbf{B}_\tau$  using the proposed estimation procedure under the AR(1) correlation structure, compute its standard error based on 500 bootstrap samples, and report in Table 2. All estimated coefficients are statistically significant, since their 95% bootstrap confidence intervals do not include zero. For  $\tau = 0.5$  and  $0.75$ , all treatment effects are beneficial, indicating that the depression scores decrease over time, since the signs of coefficients corresponding to a linear polynomial are all negative. With the proposed estimators, we plot the fitted growth curves for three groups at  $\tau = 0.25, 0.5,$  and  $0.75$  as exhibited in Figure 3. This figure indicates that all treatments are effective at reducing depression scores over a given period of time at  $\tau = 0.25$ , yet the reduction ratio is decreasing due to the positive quadratic term. This can be explained by the fact that the fitted score is getting closer to zero over time while preserving the positive value.

Table 2

Estimated coefficients and standard errors (in brackets) obtained from the proposed approach under the AR(1) structure and Koenker and Bassett's one assuming the working independence

		Proposed	K & B
$\tau = 0.25$			
Medication	Intercept	13.24 (0.20)	13.23 (0.26)
	Linear	-3.71 (0.10)	-3.76 (0.11)
	Quadratic	0.34 (0.02)	0.35 (0.02)
Psychotherapy	Intercept	12.26 (0.28)	12.27 (0.24)
	Linear	-3.72 (0.07)	-3.78 (0.09)
	Quadratic	0.42 (0.02)	0.45 (0.02)
Referral	Intercept	12.39 (0.33)	12.59 (0.30)
	Linear	-3.27 (0.11)	-3.24 (0.17)
	Quadratic	0.42 (0.02)	0.39 (0.03)
$\tau = 0.50$			
Medication	Intercept	16.01 (0.47)	15.83 (0.59)
	Linear	-1.61 (0.17)	-1.66 (0.15)
Psychotherapy	Intercept	14.84 (0.40)	14.03 (0.56)
	Linear	-1.09 (0.16)	-1.07 (0.16)
Referral	Intercept	14.28 (0.45)	14.34 (0.50)
	Linear	-0.49 (0.19)	-0.50 (0.20)
$\tau = 0.75$			
Medication	Intercept	20.55 (0.49)	20.16 (0.46)
	Linear	-1.11 (0.17)	-1.23 (0.18)
Psychotherapy	Intercept	18.51 (0.56)	18.82 (0.66)
	Linear	-0.90 (0.28)	-0.98 (0.25)
Referral	Intercept	19.51 (0.53)	19.33 (0.56)
	Linear	-0.35 (0.13)	-0.38 (0.15)



**Figure 3.** Fitted growth curves for medication (solid), psychotherapy (dashed), and referral (dotted) group at three quantiles.

In addition, Figures 1 and 3 confirm that subjects are well randomized to three groups since the fitted quantiles of the depression scores at baseline are comparable between three groups. We also fit the parsimonious model to the data using Koenker and Bassett’s approach assuming the working independence, and report the estimated coefficients and standard errors in Table 2. The results are comparable to the proposed approach, yet most of the standard errors increase.

When the treatment effects are compared, the intervention-based care for depression appears to be effective relative to referral to community care regardless of  $\tau$ , while medication and psychotherapy treatments performed similarly. Thus, we further conduct the proposed hypothesis test for comparing each pair of curves to see if they are different at each quantile level. Table 3 provides the test statistics along with p-values. We conclude at a significance level of 0.05 that the proposed test rejects the null hypothesis when medication and referral groups are compared for all three quantiles, while it fails to reject the equality between the growth curves of medication and psychotherapy group. In addition, this test fails to reject the null when psychotherapy and referral groups are compared, yet the p-value gets closer to 0.05 as the level of  $\tau$  decreases (0.259, 0.089, and 0.059 at  $\tau = 0.75, 0.5,$  and  $0.25,$  respectively). In summary, the psychotherapy intervention can be effective as compared to referral to community care at  $\tau = 0.25,$  while the medication intervention is always more beneficial regardless of the quantile level of depression.

We remark that for  $\tau = 0.75,$  the test result seems to contradict the last plot as shown in Figure 3; the null is rejected only for comparison of medication and referral groups, while the fitted linear curve for psychotherapy group is farther from the referral group’s curve than the medication group’s one. In order to reject the equality of two linear curves at  $\tau = 0.75,$  the difference between intercepts or slopes in the two lines should be statistically significant. According to Figure 3, the difference of the curves for psychotherapy and referral groups is mainly due to the gap between their estimated intercepts. However, this might not be enough to reject the equality due to a large variation of the intercepts, that is, a large standard error as shown in Table 2. This finding emphasizes the necessity of the proposed hypothesis test in the analysis of the depression study.

**4. Discussion**

Quantile regression for longitudinal data has been extensively discussed over the last few decades; see Jung (1996), He, Fu, and Fung (2003), Koenker (2004), Geraci and Bottai (2007), Yi and He (2009), Tang and Leng (2011), Wang and Zhu (2011), and Lu and Fan (2015). However, most of the aforementioned references mainly focus on estimation of quantile regression parameters under the linearity assumption between outcomes and measurement times. As shown in the analysis of the depression data of Section 3.2, this assumption could be too restrictive to describe the longitudinal trajectory of

**Table 3**

*Test statistics and p-values comparing treatment groups indicating whether or not they are same at three quantiles. Denote medication, psychotherapy, and referral groups by M, P, and R, respectively.*

$\tau$		M vs. P	P vs. R	M vs. R
0.25	$ELT_\tau$	5.992	7.440	11.678
	p-value	0.112	0.059	0.009
0.50	$ELT_\tau$	2.336	4.949	6.898
	p-value	0.311	0.084	0.032
0.75	$ELT_\tau$	2.416	2.706	8.919
	p-value	0.299	0.259	0.011

the distribution of the outcomes at a certain level of  $\tau$ . In this article, we have offered a complete process in a nonlinear quantile regression model; it provides the parsimonious growth curve model, improves estimation efficiency of quantile regression parameters, and conducts the hypothesis test to compare several groups of interest in terms of the pattern of the distribution of outcomes over time.

A polynomial growth curve model with a sufficiently high degree may fit the longitudinal data sufficiently well. However, it is not desirable in practice due to the complexity of the model and the difficulty of interpretation. We have proposed the Bayesian information criterion based on the empirical log-likelihood ratio. This model selection approach adjusts the balance between the complexity of the growth curve model and lack of fit of the data effectively by selecting the optimal degree of the polynomial curve at each quantile level. Moreover, the empirical loglikelihood ratio has been used to construct the hypothesis test for the equality of the growth curves. The proposed test can be readily extended to the model specification test for assessing whether a certain form of growth curve fits the data adequately or not.

If the polynomial growth curve model no longer provides a good fit to data, then a nonparametric model is a viable alternative. For example, a spline basis can be used in place of a polynomial in model (1) in which the number of knots is allowed to increase with the sample size. An optimal number of knots and comparison of nonparametric growth curves can be also implemented through our model selection and hypothesis test.

## 5. Supplementary Materials

Supplementary materials available at the *Biometrics* website on Wiley Online Library include R codes for Section 3.2, the regularity conditions and the theoretical proofs.

## ACKNOWLEDGEMENTS

We are very grateful to the editor, an associate editor, and a referee for their insightful comments and suggestions that have improved the manuscript significantly. In addition, we very much appreciate that Tang and Leng (2011) have provided R codes for their method.

## REFERENCES

- Cho, H., Hong, H. G., and Kim, M. O. (2016). Efficient quantile marginal regression for longitudinal data with dropouts. *Biostatistics* **17**, 561–575.
- Geraci, M. and Bottai, M. (2007). Quantile regression for longitudinal data using the asymmetric Laplace distribution. *Biostatistics* **8**, 140–154.
- He, X., Fu, B., and Fung, W. K. (2003). Median regression for longitudinal data. *Statistics in Medicine* **22**, 3655–3669.
- Jung, S. (1996). Quasi-likelihood for median regression models. *Journal of the American Statistical Association* **91**, 251–257.
- Koenker, R. (2004). Quantile regression for longitudinal data. *Journal of Multivariate Analysis* **91**, 74–89.
- Koenker, R. and Bassett, G. (1978). Regression quantiles. *Econometrica* **46**, 33–50.
- Liang, K. Y. and Zeger, S. L. (1986). Longitudinal data analysis using generalised linear models. *Biometrika* **73**, 12–22.
- Lu, X. and Fan, Z. (2015). Weighted quantile regression for longitudinal data. *Computational Statistics* **30**, 569–592.
- Miranda, J., Chung, J. Y., Green, B. L., Krupnick, J., Siddique, J., Revicki, D. A., et al. (2003). Treating depression in predominantly low-income young minority women: A randomized controlled trial. *The Journal of American Medical Association* **290**, 57–65.
- Owen, A. B. (2001). *Empirical likelihood*. New York: Chapman and Hall-CRC.
- Potthoff, R. F. and Roy, S. N. (1964). A generalized multivariate analysis of variance model useful especially for growth curve problems. *Biometrika* **51**, 313–326.
- Qin, J. and Lawless, J. (1994). Empirical likelihood and general estimating equations. *The Annals of Statistics* **22**, 300–325.
- Qu, A., Lindsay, B. G., and Li, B. (2000). Improving generalised estimating equations using quadratic inference functions. *Biometrika* **87**, 823–836.
- Tang, C. Y. and Leng, C. (2011). Empirical likelihood and quantile regression in longitudinal data analysis. *Biometrika* **98**, 1001–1006.
- Wang, H., Li, R., and Tsai, C. L. (2007). Tuning parameter selectors for the smoothly clipped absolute deviation method. *Biometrika* **94**, 553–568.
- Wang, H. and Zhu, Z. (2011). Empirical likelihood for quantile regression models with longitudinal data. *Journal of Statistical Planning and Inference* **141**, 1603–1615.
- Yi, G. and He, W. (2009). Median regression models for longitudinal data with dropouts. *Biometrics* **65**, 618–625.
- Zhou, J. and Qu, A. (2012). Informative estimation and selection of correlation structure for longitudinal data. *Journal of the American Statistical Association* **107**, 701–710.

Received July 2016. Revised September 2017.  
Accepted September 2017.