行政院國家科學委員會專題研究計畫 成果報告

參考曲線之比較
研究成果報告(精簡版)

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執 行 單 位 ：國立交通大學統計學研究所

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處 理 方 式 ：本計畫可公開查詢

中 華 民 國 100 年 10 月 27 日

Report for NSC Research Project

Project title: Hypothesis Testing for Equality of Reference Charts
Project number: NSC 99-2118M-009-002
Investigator: Lin-An Chen, Institute of Statistics, National Chiao Tung University

Contents:

1. Reserach Report

A. Introduction and Paper Review

Growth is a fundamental property of biological systems, occurring at the level of populations, individual animals and plants, as well as within organisms while the growth of a subject depends on nutritional, health, and environmental conditions. Typically the growth pattern for a treatment group depicts a family of symmetric quantile curves, called reference charts, as a function of some covariates (age or time). One difficulty in reference charts problem is that the measurement variables taken over time are generally not independent.

Much research has been devoted to modelling growth function and constructing growth charts in parametric or nonparametric way. For overview of parametric methodology, linear or nonlinear growth models, see Cole and Green (1992) and Laird and Ware (1982). When the measurements

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can be formulated as parametric regression model, the reference charts may be expressed as simple functions of parameters involved in the regression model so that its estimation may be done through estimations of these parameters. For example, the reference charts of a regression with normal errors model are linear functions of the mean and standard deviation. For growth characteristics that are approximately normal, proposals are available for transformations to normal where, among them, the most successful proposal is the LMS by Cole (1988). However, the Exponential-Normal distribution method by Wright and Royston (1997) has the advantage of being parametric with explicit expressions for estimating parameters and quantiles.

Verifying the similarity of two growth patterns through comparing the reference charts is an important topic in application. Basically the use of growth charts tries to summarize individual differences in the growth pattern and it is commonly known that the comparison of reference charts is done by studying the determinants of these differences. The most common method of comparison considers parametric growth model that the determinals of growth pattern can be represented by a few model parameters so that the job can be done by comparison of these parameters. However, the reference charts comparison considered in literature mainly restrcited on the comparison of growth regression functions. For example, it is seen that most parametric comparison methods consider only those parameters involved in regression function such as testing equality of two or several regression parameter vectors (see, Hoel (1964), Chi and Weerahandi (1998) and Pan and Cole (2004)) or comparing relations between regression slope parameters and (or) intercept parameters (see Zucker, Zerbe and Wu (1995)). Instead of parametric reference charts comparison, there are nonparametric methods comparing the unknown regression functions (see, for examples, Scheike and Zhang (1998), Scheike, Zhang and Juul (1999), Richard, et al. (1989) and Griffiths, Iles et al. (2004)). Hoel (1964) showed that such methods are less efficient than those to compare values of regression parameters.

For any comparison exercise, there needs to be clarity its precise objectives. For that assessment of growth pattern by charts is the single tool for defining health and nutritional status at both individual and population (country) level, there needs more general study for public health purpose in verifying if two or several countries display in the same or similar growth pattern. In light of this, we may ask: Do two populations (countries) have the same reference charts? This is an objective important to be answered in public health, espectially, for studying the developing countries. However, little research has been performed in reference charts comparison truely investigated in this purpose. It can be seen that comparisons of mean regression functions or few regression parameters can not achieve this public health problem (see Henry (1992)). One exception of a closer study is that Heckman and Zamar (2000) discussed the concepts of similarity and grouping in growth pattern based on rank correlation coefficient between regression functions. However, besides this is an estimation procedure that it is difficult to extend to hypothesis testing of comparison, regression function comparison is not enough to interprete the similarity or equality of growth patterns characterized by the reference charts.

B. Research Purpose

We consider the unknown population reference charts as parameters and study the differnces of two sets of unknown reference charts for comparison. This generalizes the comparison problem to a more general growth patterns comparison. With this aim, we develop the analytic relationships between model parameters of growth models achieving the fact of equality of population reference charts. This relationships provides exact test for comparison of reference charts and this observation indicates that testing equalities of regression parameters or regression mean functions often provides only a crude approximation to reality so that the conclusions for growth pattern comparison are very questionable. This approach is heading in a right direction in a general investigation if two growth models are with the same growth pattern.

In this paper, we develop parameter relations for equality of reference charts constructed for two linear growth models that covers most linear mixed effects models. We then select several interesting longitudinal linear models as examples to display these relations. These results will show that all existed studies of comparisons of regression parameters even without assuming known structure of covariance matrix of error variables are inappropriate. Finally, we propose an exact test for conducting comparison of reference charts.

C. Reserach Methods

We state the idea of transforming the equality of two group of reference charts into equality of functions of two group of regression parameters.

We consider that the response variable has a population type linear regression model

$$y(t) = x(t)'\beta_y + \epsilon_y(t), t \in (0,1) \tag{1}$$

where $x(t)$ is vector of independent variables indexd in t and $\epsilon_y(t)$ is error variable with mean zero. In practice, we have a samples of $y(t)$ and $x(t)$ for t being $t_1, ..., t_n$ for inferences. Suppose that for another group of subjects there is also a response variable $z(t)$ that follows the same linear regression model with possibly different parameters as

$$z(t) = x(t)'\beta_z + \epsilon_z(t) \tag{2}$$

where $\epsilon_z(t)$ is also error variable independent of $\epsilon_y(t)$ with mean zero. Using the same explanatory variables $x(t)$ indicates the balanced design that all the subjects in two groups are measured on the same set of time points.

The general form of the reference charts is a series of smoothed curves, selected quantiles of the distribution of the response variable, plotted against the covariate (age or time). For $\gamma \in (0,1)$, the conditional quantile of y given age t is denoted by $F_y^{-1}(\gamma|t)$. The γth reference curve is the plot of the function $F_y^{-1}(\gamma|t)$ against t in S, set of ages, that can be reprented as

$$C_y(\gamma) = \{F_y^{-1}(\gamma|t) : t \in S\}$$

where S is the set of age. The reference curves of 7 percentages, $\gamma = 0.05, ..., 0.95$, symmetrical above and below the median, are used in North American and Europe. It is no loss of generality to consider all percentages in $(0, 1)$. Without specifying the quantile percentages $\gamma's$, we consider the reference curves for a population of variable y as

$$\{C_y(\gamma) : \gamma \in (0, 1)\}.$$

For response variable $z(t)$, the γth reference chart may be analogously represented as

$$C_z(\gamma) = \{F_z^{-1}(\gamma|t) : t \in S\}$$

where $F_z^{-1}(\gamma|t)$ is the γth quantile of z at time t and the reference charts for the population of variable z is $\{C_z(\gamma) : \gamma \in (0, 1)\}$. The general hypothesis for comparison of reference charts then is

$$H_0 : C_y(\gamma) = C_z(\gamma), \gamma \in (0, 1).$$

With linear model assumption of (1), it is seen that the γth reference charts may be written as $F^{-1}_{y(t)|x(t)}(\gamma) = x(t)'\beta_y + F^{-1}_{\epsilon_y}(\gamma) = x(t)'\beta_{y\gamma}$ where $\beta_{y\gamma} = \beta_y + \begin{pmatrix} F^{-1}_{\epsilon_y}(\gamma) \\ 0_{p-1} \end{pmatrix}$ is called the regression quantile (see Koenker and Bassett (1978)). The 100γ%th reference chart then is

$$C_y(\gamma) = \{x(t)'\beta_{y\gamma} : t \in S\}.$$

The γth regression quantile for model (2) is $F^{-1}_{z(t)}(\gamma) = x(t)'\beta_z + F^{-1}_{\epsilon_z}(\gamma) = x(t)'\beta_{z\gamma}$ with $\beta_{z\gamma} = \beta_z + \begin{pmatrix} F^{-1}_{\epsilon_z}(\gamma) \\ 0_{p-1} \end{pmatrix}$. Then the γ reference chart for response variable z is

$$C_z(\gamma) = \{x(t)'\beta_{z\gamma} : t \in S\}.$$

and then the reference charts for regression model (2) is

$$\{C_z(\gamma) : \gamma \in (0, 1)\}.$$

Hence, equality of reference charts is identical to $C_y(\gamma) = C_z(\gamma)$ for $\gamma \in (0, 1)$. This establish a rule for verification of equality of two group of reference charts.

D. Results and Discussion

The major theorem is stated below.

Theorem. (a) The hypothesis of equal reference charts may be formulated as

$$H_{ref} : \beta_y = \beta_z, F_{\epsilon_y}^{-1}(\gamma) = F_{\epsilon_z}^{-1}(\gamma),\ \gamma \in (0, 1).$$

(b) If we further assume that $F_{\epsilon_y}^{-1}(\gamma) = \sigma_y F_0^{-1}(\gamma)$ and $F_{\epsilon_z}^{-1}(\gamma) = \sigma_z F_0^{-1}(\gamma)$ where σ_y and σ_z are two unknown constants not dependent of time t. Then the hypothesis reduces to

$$H_{ref} : \beta_y = \beta_z, \sigma_y = \sigma_z.$$

Result of (b) in Theorem tells us that solving a comparison of reference charts is valid to be treated as a problem of testing hypothesis for equalities of some model parameters. However, different growth models lead to varying hypothesis testing problems.

The random intercept model

The random intercept model for one individual is of the form

$$y(t_j) = \beta_{0y} + V_y + \beta_{1y} x_1(t_j) + \delta_y(t_j), j = 1, ..., n$$

where V_y has normal distributions $N(0, \sigma_{vy}^2)$ and $\delta_y(t_j)'s$ are independent normal distributions $N(0, \sigma_y^2)$. The equality of reference charts indicates

$$\beta_{0y} + \beta_{1y} x_1(t) + \sqrt{\sigma_{vy}^2 + \sigma_y^2} z_\gamma = \beta_{0z} + \beta_{1z} x_1(t) + \sqrt{\sigma_{vz}^2 + \sigma_z^2} z_\gamma$$
$$\text{for all } x_1(t) \text{ and } \gamma \in (0, 1)$$

which indicates that testing equalities of reference charts is equivalent to test the following hypothesis

$$H_{ref} : \beta_y = \beta_z, \sqrt{\sigma_y^2 + \sigma_{vy}^2} = \sqrt{\sigma_z^2 + \sigma_{vz}^2}.$$

The autoregressive model

The sample autoregressive model is model with error variables of the form

$$y(t_j) = \beta_{0y} + \beta_{1y} x_1(t_j) + \epsilon_y(t_j), j = 1, ..., n$$
$$\epsilon_y(t_j) = \rho_y \epsilon_y(t_{j-1}) + \delta_y(t_j)$$

where $\delta_y(t_j)$'s are iid random variables with normal distribution $N(0, \sigma_y^2)$. Then the set of reference charts is

$$C_y(\gamma) = \{\beta_{0y} + \beta_{1y}x_1(t) + \sqrt{\frac{\sigma_y^2}{1-\rho_y^2}}z_\gamma : t \in S\}.$$

Hence, the equality of reference charts indicates

$$\beta_{0y} + \beta_{1y}x_1(t)\sqrt{\frac{\sigma_y^2}{1-\rho_y^2}}z_\gamma = \beta_{0z} + \beta_{1z}x_1(t) + \sqrt{\frac{\sigma_z^2}{1-\rho_z^2}}z_\gamma$$
for all $x_1(t)$ and $\gamma \in (0, 1)$

which requires to test the following hypothesis

$$H_{ref} : \beta_y = \beta_z, \sqrt{\frac{\sigma_y^2}{1-\rho_y^2}} = \sqrt{\frac{\sigma_z^2}{1-\rho_z^2}}.$$

Random slope model

A simple random slope effects model is

$$y(t_j) = \beta_{0y} + (\beta_{1y} + B_y)x_1(t_j) + a_y(t_j), j = 1, ..., n$$

where B_y is a random variable with mean zero and variance $\sigma_{\delta y}^2$ and $a_y(t)$'s are iid random variables with mean zero and variance σ_y^2. The the set of reference charts is

$$C_y(\gamma) = \{\beta_{0y} + \beta_{1y}x_1(t) + \sqrt{\sigma_{\delta y}^2 x_1(t)^2 + \sigma_y^2}z_\gamma : t \in S\}.$$

Then, the equality of reference charts indicates

$$\beta_{0y} + \beta_{1y}x_1(t) + \sqrt{\sigma_{\delta y}^2 x_1(t)^2 + \sigma_y^2}z_\gamma = \beta_{0z} + \beta_{1z}x_1(t) + \sqrt{\sigma_{\delta z}^2 x_1(t)^2 + \sigma_z^2}z_\gamma$$
for all $x_1(t)$ an d $\gamma \in (0, 1)$

which requires to test the following hypothesis

$$H_{ref} : \beta_y = \beta_z, \sigma_{\delta y} = \sigma_{\delta z}, \sigma_y = \sigma_z. \quad \square$$

Tests for hypotheses stated here are developed in this paper and evaluation of power of these tests are also decribed.

2. References

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3. Self Evaluation

The results established in this paper allows the practioners to truely verify if a population of people has a growth pattern the same as the growth pattern of another population of people. The WHO is deeply concerned the child's growths of African or other developing countries. The methods and methods in this paper provide correct techniques for this need of investigation.

國科會補助計畫衍生研發成果推廣資料表

日期:2011/10/26

國科會補助計畫	計畫名稱: 參考曲線之比較	
	計畫主持人: 陳鄰安	
	計畫編號: 99-2118-M-009-002-	學門領域: 數理統計

無研發成果推廣資料

99 年度專題研究計畫研究成果彙整表

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其他成果 (無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。)	No

	成果項目	量化	名稱或內容性質簡述
科教處計畫加填項目	測驗工具(含質性與量性)	0	
	課程/模組	0	
	電腦及網路系統或工具	0	
	教材	0	
	舉辦之活動/競賽	0	
	研討會/工作坊	0	
	電子報、網站	0	
	計畫成果推廣之參與（閱聽）人數	0	

國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

■達成目標

□未達成目標（請說明，以 100 字為限）

□實驗失敗

□因故實驗中斷

□其他原因

說明：

2. 研究成果在學術期刊發表或申請專利等情形：

論文：□已發表 ■未發表之文稿 □撰寫中 □無

專利：□已獲得 □申請中 ■無

技轉：□已技轉 □洽談中 ■無

其他：（以 100 字為限）

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）（以 500 字為限）

當我們想了解本國孩童成長型態是否與先進國家孩童成長型態是否相同，我們就必須比較兩國孩童之參考圖是否相同。我們建立參考圖相同之迴歸參數表示式，這個表示式讓我們藉由參數之比較就可達到檢定參考圖相等之假設。這大大的簡化公共衛生方面的重要工作。這對世界衛生組織從事研究，了解落後國家孩童營養、生長狀態等均有莫大幫助。