Individual Growth Models of Change in Peabody Picture Vocabulary Scores of Children Treated for Brain Tumors

Ying Shen

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INDIVIDUAL GROWTH MODELS OF CHANGE IN PEABODY PICTURE VOCABULARY SCORES OF CHILDREN TREATED FOR BRAIN TUMORS

by

Ying Shen

Under the Direction of Yu-Sheng Hsu

ABSTRACT

The individual growth model is a relatively new statistical technique. It is now widely used to examine the trajectories of individuals and groups in repeated measures data. This study examines the association of the receptive vocabulary over time and characteristics of children who were treated for brain tumors. The children undertook different types of treatment from one to any combinations of surgery, radiation and chemotherapy. The individual growth model is used to analyze the longitudinal data and to address the issues behind the data. Results of this study present several factors’ influences to the rate of change of PPVT scores. The conclusions of this thesis indicate that the decline in the PPVT scores is associated with gender, age at diagnosis, socioeconomic status, type of treatment and Neurological Predictor Scale.

INDEX WORDS: Longitudinal data, Individual growth model, Fractional polynomial transformation
INDIVIDUAL GROWTH MODELS OF CHANGE IN PEABODY PICTURE VOCABULARY SCORES OF CHILDREN TREATED FOR BRAIN TUMORS

by

Ying Shen

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of

Master of Science

in the College of Arts and Sciences

Georgia State University

2007
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by

Ying Shen

Major Professor: Dr. Yu-Sheng Hsu
Committee: Dr. Tricia King
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Electronic Version Approved:

Office of Graduate Studies
College of Art and Sciences
Georgia State University
December 2007
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Tables</td>
<td>viii</td>
</tr>
<tr>
<td>List of Figures</td>
<td>x</td>
</tr>
<tr>
<td>List of Abbreviations</td>
<td>xi</td>
</tr>
<tr>
<td>Chapter One: Introduction</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Background</td>
<td>1</td>
</tr>
<tr>
<td>1.2 Source of data</td>
<td>2</td>
</tr>
<tr>
<td>1.3 Method of analysis</td>
<td>5</td>
</tr>
<tr>
<td>Chapter Two: Methodology</td>
<td>6</td>
</tr>
<tr>
<td>2.1 The Hierarchical Linear Model (HLM)</td>
<td>6</td>
</tr>
<tr>
<td>2.2 Fractional Polynomial Transformation</td>
<td>8</td>
</tr>
<tr>
<td>2.3 Statistical analysis</td>
<td>9</td>
</tr>
<tr>
<td>2.3.1 Individual Growth Models for Treatments and other variables</td>
<td>10</td>
</tr>
<tr>
<td>2.3.2 Individual Growth Models for Neurological Predictor Scale and other variables</td>
<td>20</td>
</tr>
<tr>
<td>Chapter Three: Results and Discussion</td>
<td>30</td>
</tr>
<tr>
<td>3.1 Models for treatments and other variables</td>
<td>30</td>
</tr>
<tr>
<td>3.1.1 Model without interactions</td>
<td>30</td>
</tr>
<tr>
<td>3.1.2 Model with interactions</td>
<td>30</td>
</tr>
<tr>
<td>3.1.3 Model with variable transformation</td>
<td>31</td>
</tr>
<tr>
<td>3.2 Models for Neurological Predictor Scale and other variables</td>
<td>32</td>
</tr>
<tr>
<td>3.2.1 Model without interactions</td>
<td>32</td>
</tr>
</tbody>
</table>
3.2.2 Model with interactions ....................................... 33
3.1.3 Model with variable transformation .......................... 33

Chapter Four: Conclusion and Future Research.............................. 35
References................................................................................. 36
Appendix A: SAS Code .............................................................. 38
Appendix B: Models for time beginning from diagnosis date .............. 57
List of Tables

Table 1.1: Descriptive Table of Treatments, Gender, Age at diagnosis and SES classes .......................................................... 3

Table 1.2: Descriptive Table of PPVTSS, NPS_total, and Time ......................... 4

Table 1.3: Time point count distribution .......................................................... 4

Table 2.1: Solution for fixed effects ................................................................. 10

Table 2.2: Fixed effects for the model without interactions for the treatments and other variables ............................................................. 11

Table 2.3: Random effects for the model without interactions for the treatments and other variables ............................................................. 11

Table 2.4: Fixed effects for the model with interactions for the treatments and other variables ............................................................. 13

Table 2.5: Random effects for the model with interactions for the treatments and other variables ............................................................. 14

Table 2.6: Results of fractional polynomial transformation for SES, age at diagnosis and time ............................................................. 15

Table 2.7: Results of testing the significance of variables ..................................... 16

Table 2.8: Fixed effects for the model with variable transformation for the treatments and other variables ............................................................. 17

Table 2.9: Random effects for the model with variable transformation for the treatments and other variables ............................................................. 17
Table 2.10: Fixed effects for the model without interactions for Neurological Predictor Scale and other variables ........................................ 20
Table 2.11: Random effects for the model without interactions for Neurological Predictor Scale and other variables ...................... 21
Table 2.12: Fixed effects for the model with interactions for Neurological Predictor Scale and other variables ....................... 23
Table 2.13: Random effects for the model with interactions for Neurological Predictor Scale and other variables ..................... 23
Table 2.14: Results of testing the significance of Neurological Predictor Scale .................................................................................. 26
Table 2.15: Fixed effects for the model with variable transformation for Neurological Predictor Scale and other variables .............. 27
Table 2.16: Random effects for the model with variable transformation for Neurological Predictor Scale and other variables .............. 27
Table 3.1: Comparison of models for treatments and other variables ......... 32
Table 3.2: Comparison of models for Neurological Predictor Scale and other variables .......................................................... 34
List of Figures

Figure 1.1: Individual PPVT score trajectories ........................................ 5
Figure 2.1: Individual grow curves for some categories using model
without interactions for treatments and other variables ........... 12
Figure 2.2: Individual grow curves for some categories using model
with interactions for treatments and other variables .............. 14
Figure 2.3: Individual grow curves for some categories using model
with variable transformation for treatments and other variables.. 18
Figure 2.4: Individual growth curves for treatment and other variables .... 19
Figure 2.5: Individual grow curves for some categories using model
without interactions for Neurological Predictor Scale and
other variables ................................................................. 22
Figure 2.6: Individual grow curves for some categories using model
with interactions for Neurological Predictor Scale and
other variables ................................................................. 24
Figure 2.7: Individual grow curves for some categories using model
with variable transformation for Neurological Predictor Scale and
other variables ................................................................. 28
Figure 2.8: Individual growth curves for Neurological Predictor Scale
and other variables ............................................................. 29
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES</td>
<td>Socioeconomic Status</td>
</tr>
<tr>
<td>PPVTSS</td>
<td>Peabody Picture Vocabulary Test Standard Scores</td>
</tr>
<tr>
<td>NPS_CH</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>NPS_Rad</td>
<td>Radiation</td>
</tr>
<tr>
<td>NPS_total</td>
<td>Neurological Predictor Scale</td>
</tr>
</tbody>
</table>
Chapter One: Introduction

1.1 Background

Brain tumors are a life-threatening and chronic ailment for many children and comprise approximately 22% of childhood cancers and tumors originating in the central nervous system, and are the second only to leukemia in cause of death among childhood cancers [1, 2]. The standard treatments for brain tumors are surgery, radiation therapy, chemotherapy, and any combinations of the three treatments.

Surgery is the primary form of treatment for brain tumors that lie within the membranes covering the brain or in parts of the brain that can be removed without damaging critical neurological functions. Because a tumor is likely to recur if any tumor cells are left behind, the goal of surgery is to remove the entire tumor whenever possible. It is frequently used in combination with other intervention when necessary [3].

Radiation therapy and chemotherapy are generally used as secondary or adjuvant treatments for tumors that cannot be managed using only surgery. However, radiation and chemotherapy may be used without surgery if the tumor is inoperable. Radiation therapy uses high-energy x-rays or other types of ionizing radiation to stop cancer cells from dividing. Because the developing brain of a child is very sensitive to radiation therapy, it is deliberately limited [3]. Chemotherapy required for the more aggressive tumors uses chemicals (drugs) that have a toxic effect on tumor cells as they divide. Survival rates of children with certain types of brain tumors have been significantly improved by the treatment of radiation therapy and chemotherapy.
The children who have undergone treatment for brain tumors which have direct impact on crucial brain structures underlying behavior may be more likely to exhibit behavior problems than their peers. Although studies have found that survivors are at risk for a variety of physical, medical, cognitive, and/or psychosocial late effects, the particular risk factors having an impact on children’s psychosocial and behavioral functioning are not fully understood. These late effects may be directly related to the type of treatment (surgery, chemotherapy, and/or radiation), characteristics of the disease (tumor size and type), and individual demographic factors, such as age and socioeconomic status [4].

1.2 Source of Data

The data for this study comes from a longitudinal study conducted by Robin Morris of Georgia State University over 15 years ago. Trica King in collaboration with Robin Morris and other researchers are evaluating the survivors of childhood brain tumors from the original longitudinal study when began at the time when they undertook diagnosis and treatments. Drs. Tricia King and Robin Morris (Department of Psychology) and along with Dr. Yu-Sheng Hsu (Mathematics and Statistics Department) are conducting studies to identify the predictors of longitudinal data such as the PPVT [5]. Peabody Picture Vocabulary Test (PPVT) is a measure of receptive vocabulary for Standard English and a screening test of verbal ability. In this study, we analyzed change in PPVT scores over time in these children.

Between 1985 and 1996, 98 patients participated in the longitudinal study and 93 out 98 patients’ information were complete. The patients’ data include PPVT scores,
date of birth of the participant, gender, socioeconomic status, treatments the patient undertook, Neurological Predictor Scale the patient had, date of the diagnosis, and date of taking PPVT test. The age of diagnosis of those 93 patients is ranged from 0.4 to 16.7 years old. The Neurological Predictor Scale is ranged from 2 to 11. The range of observation per patient is from 1 to 11.

Table 1.1: Descriptive Table of Treatments, Gender, and SES classes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
<th></th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>with</td>
<td>without</td>
<td>with</td>
</tr>
<tr>
<td>Surgery</td>
<td>79</td>
<td>14</td>
<td>391</td>
</tr>
<tr>
<td>Chemo</td>
<td>25</td>
<td>68</td>
<td>138</td>
</tr>
<tr>
<td>Radiation</td>
<td>62</td>
<td>31</td>
<td>283</td>
</tr>
<tr>
<td>Male</td>
<td>50</td>
<td></td>
<td>235</td>
</tr>
<tr>
<td>Female</td>
<td>43</td>
<td></td>
<td>198</td>
</tr>
<tr>
<td>Age&lt;=7 years old</td>
<td>58</td>
<td></td>
<td>306</td>
</tr>
<tr>
<td>Age&gt;7 years old</td>
<td>35</td>
<td></td>
<td>127</td>
</tr>
<tr>
<td>SES classes</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>19</td>
<td>23</td>
</tr>
</tbody>
</table>

The potentially predictive variables included in this study are gender, age at diagnosis, Socioeconomic Status Class (SES), surgery, chemotherapy, radiation, time since treatment and Neurological Predictor Scale (NPS_total). A family's socioeconomic status is based on family income, parental education level, and parental occupation. There are five levels for SES class in which class 1 is the highest level and
class 5 is the lowest level. Neurological Predictor Scale (NPS_total) is a nonratio, ordinal scale. It is a sum of patients’ rated scores across 4 domains which are tumor-related conditions, operative events, radiation treatment, and chemotherapy [6].

Table 1.2: Descriptive Table of PPVTSS, NPS_total, Age at diagnosis and Time

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPVT Standardized Score</td>
<td>89.2909931</td>
<td>19.5685721</td>
<td>40 to 132</td>
</tr>
<tr>
<td>Neurological Predictor Scale</td>
<td>6.2494226</td>
<td>2.0610263</td>
<td>2 to 11</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>5.7768538</td>
<td>3.5683538</td>
<td>0.4 to 16.7</td>
</tr>
<tr>
<td>Time(years between treatment and measurement)</td>
<td>2.6656600</td>
<td>3.5572518</td>
<td>0 to 15.9</td>
</tr>
</tbody>
</table>

The data consisted of 433 records on 93 individuals. The frequency distribution of the number of time points is seen in Table 1.3. The data on 45 children who have more than two time points are displayed graphically in Fig. 1.1.

Table 1.3: Time point count distribution

<table>
<thead>
<tr>
<th>Number of Time Points</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>40.86</td>
<td>40.86</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>10.75</td>
<td>51.61</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>8.61</td>
<td>60.22</td>
</tr>
<tr>
<td>More than 3</td>
<td>37</td>
<td>39.78</td>
<td>100.00</td>
</tr>
</tbody>
</table>
1.3 Method of Analysis

In order to analyze change over time in psychological studies, there are numerous traditional methods that can be applied. These include the mixed model analysis of variance (ANOVA) and the multivariate approach to repeated measures (MANOVA), the analysis of covariance (ANCOVA) or residualized change analysis, and the analysis of covariance with reliability correction (ANCOVARC).

In this study, we will use individual growth model to analyze the changes over time in PPVT data. Much study shows that it is both possible and desirable to model change at the individual level [7]. The individual growth model is a relative new statistical technique now widely used to examine the unique trajectories of individuals and groups in repeated measures data.
Chapter Two: Methodology

In this chapter, the individual growth models we get are presented. Since repeated measurements were taken on each child obtained over time, hierarchical linear models were used for the analysis of change. To explain the change over time of standard scores of PPVT, two sets of variables were considered. One set includes Years between date of treatment and date of exam (Time), Gender, Age at diagnosis, SES classes, Treatments (surgery, radiation and chemotherapy), and potential interactions of these variables. The other one consists of Years between date of treatment and date of exam (Time), Gender, Age at diagnosis, SES classes, Neurological Predictor Scale (NPS_total), and potential interactions of these variables. The patients are assumed to be random and other variables are fixed effects in the model. Fractional polynomial transformation was applied in this study for the continuous variables.

2.1 The Hierarchical Linear Model (HLM)

Longitudinal studies sometimes known as repeated measures are encountered in a wide variety of disciplines. Longitudinal data is the union of cross-sectional and time series data. The balanced design in longitudinal data analysis assumes a complete data set with an equal number of measurements over time for each subject, while the unbalanced design has incomplete data without equal time intervals or time points for each subject [8, 9]. Literature shows that hierarchical linear model (HLM) can be employed in longitudinal data analysis.
When HLM is applied to longitudinal data analysis, the level 1 units are the repeated measures for each subject and the level 2 units consist of subjects. The repeated measures are conceived as nested within each subject. The level 1 model includes time or/and quadratic time as the predictor(s). The within-subject model is:

$$ Y_{it} = \pi_{0i} + \pi_{1i} T_{it} + e_{it} $$  

By convention, within person effects are indicated by the symbol $\pi$. $Y_{it}$ represents the outcome for individual $i$ measured at time $t$. $T_{it}$ represents time from the base line assessment for person $i$. The slope $\pi_{1i}$ is the linear growth rate for the $i^{th}$ person. The intercept, $\pi_{0i}$, represents the expected outcome of the person at baseline, also called initial status. The within-person residuals, $e_{it}$, are assumed $N(0, \sigma^2)$.

At level 2, the goal is to investigate variations in the estimates of intercept and slopes in level 1 model. The between-subjects models are:

$$ \pi_{0i} = \beta_{00} + \beta_{01} x_{ti} + \ldots + \beta_{0p-1} x_{p-1,ti} + u_{0i} $$

$$ \pi_{1i} = \beta_{10} + \beta_{11} x_{ti} + \ldots + \beta_{1p-1} x_{p-1,ti} + u_{1i} $$

Accordingly, $\beta_{00}$ and $\beta_{10}$ represent the expected baseline and slope, respectively.

The coefficients for the predictors indicate how much these expected values increase or decrease. The random effects at level 2, $u_{0i}$ and $u_{1i}$ are assumed to be

$$ \begin{bmatrix} u_{0i} \\ u_{1i} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma^2_{00} & \sigma^2_{01} \\ \sigma^2_{01} & \sigma^2_{11} \end{bmatrix} \right) $$

Substitute Equation (2) into (1), we can reduce the 2-level model.
2.2 Fractional Polynomial Transformation

Fractional polynomial transformation was developed by Royston and Altman [10]. In order to determine what the value of $p$, the exponent of $x^p$ yields the best model for the covariate, Royston and Altman proposed replacing full maximum likelihood estimation of power by a search through a small but reasonable set of possible values.

For a single continuous covariate, the transformation procedure is

$$f(x, \beta) = \beta_0 + x\beta_1$$

Where $\beta$ denotes the vector of model coefficients. One way to generalize this function is to specify it as

$$f(x, \beta) = \beta_0 + \sum_{j=1}^{J} F_j(x)\beta_j$$

The functions $F_j(x)$ are a particular type of power function. The value of the first function is $F_1(x) = x^{p_0}$. The remaining functions are defined as

$$F_j(x) = \begin{cases} x^{p_j}, & p_j \neq p_{j-1} \\ F_{j-1}(x)\ln(x), & p_j = p_{j-1} \end{cases} \quad \text{for } j = 2, ..., J$$

The power can be any number, in most applied settings it is among those in the set $P = \{-2, -1, -0.5, 0, 0.5, 1, 2, 3\}$. The value $p_j = 0$ denotes the log of variable.

Implementation of the method requires, for $J = 1$, 8 models from $p_1 \in P$ are fitted. The best model is the one with the largest log likelihood. For $J = 2$, 36 models form the distinct pairs of powers, $(p_1, p_2) \in P \times P$ are fitted. Again the best model is the one with the largest log likelihood.
The relevant question is whether either of the two best models is significantly better than the linear model. The partial likelihood ratio test is used to test it. For $J = 1$,

$$G(1,p_1) = -2\{L(1) - L(p_1)\}$$

Where $L(1)$ denotes the log likelihood for the linear model and $L(p_1)$ denotes the log likelihood for the best $J = 1$ model. This partial likelihood test statistic is approximately distributed as $\chi^2$ with 1 degree of freedom under the null hypothesis of linearity in $x$.

For $J = 2$,

$$G(p_1,(p_1,p_2)) = -2\{L(p_1) - L(p_1,p_2)\}$$

Where $L(p_1,p_2)$ denotes the log likelihood for the best $J = 2$ model. This partial likelihood test statistic is approximately distributed as $\chi^2$ with 2 degree of freedom under the null hypothesis that the second function is equal to zero.

### 2.3 Statistical Analysis

SAS PROC MIXED provides a very flexible environment in which to model many types of repeated measures data. It allows the growth parameters for each individual to be examined as random effects in the model. Individual-level covariates can be entered into the model as fixed effects to determine their impact on the dependent variable alone and in interaction with the growth parameters. The structure of the variance-covariance matrix of the repeated measurements can also be examined and entered into the model. In this study, proc mixed is used to build individual growth models on two set of predictors.
2.3.1 Individual Growth Models for Treatments and other variables

The variables interested are Years between date of treatment and date of exam (Time), Gender, Age group, SES classes, Treatments (surgery, radiation and chemotherapy). The patients are divided into two age groups according to the age of diagnosis at cutting point seven-year-old. Based on Surgery (0=No, 1=Yes), Chemotherapy (0=No, 1=Yes), Radiation (0=No, 1=Yes), Age group (0: age at diagnosis is less than 7 years old, 1: otherwise), Gender (1=Female, 0=Male), and SES class (1, 2, 3, 4, 5), 160 categories are defined.

Quadratic Time is considered as a potential predictor in the first two models in order to investigate the quadratic change in PPVT scores. In the first model, only single terms are analyzed. Table 2.1 shows the solution for fixed effects for the initial step of model building.

| Effect     | Standard Effect | Estimate | Std Error | DF  | Pr > |t| |
|------------|-----------------|----------|-----------|-----|------|---|
| Intercept  |                 | 110.67   | 7.8946    | 45  | <.0001 | |
| time       |                 | -3.3137  | 1.0105    | 32  | 0.0011 | |
| time_sq    |                 | 0.2037   | 0.08930   | 25  | 0.0231 | |
| SES        |                 | -5.8808  | 1.3023    | 322 | <.0001 | |
| agegr      |                 | 8.1566   | 3.8134    | 322 | 0.0379 | |
| Surgery    |                 | -0.7040  | 5.1393    | 322 | 0.8917 | |
| NPS_Ch     |                 | -2.8210  | 3.6591    | 322 | 0.4448 | |
| NPS_Rad    |                 | -0.5594  | 4.2634    | 322 | 0.8962 | |
| Genderf    |                 | 1.6664   | 3.1643    | 322 | 0.6010 | |

Based on this initial model, backward variable selection is used to obtain the final model. All the variables in the final model are at 0.05 significant levels. Table 2.2
shows the solution for fixed effects of the final model. The variables, surgery, chemotherapy, radiation and gender are not included since they are not significant effects. Table 2.3 presents the random effects which is the variances of the intercept, linear slope and quadratic slope.

Table 2.2: Fixed effects for the model without interactions for treatments and other variables

| Effect    | Estimate | Error  | DF  | Pr > |t| |
|-----------|----------|--------|-----|-------|
| Intercept | 108.67   | 4.2888 | 49  | <.0001|
| time      | -3.4005  | 0.9075 | 379 | 0.0002|
| time_sq   | 0.1995   | 0.0745 | 379 | 0.0078|
| SES       | -5.6309  | 1.1189 | 49  | <.0001|
| agegr     | 8.7254   | 3.6458 | 49  | 0.0206|

Table 2.3: Random effects for the model without interactions for treatments and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Value</th>
<th>Pr Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN(1, 1)</td>
<td>126.26</td>
<td>38.5125</td>
<td>3.28</td>
<td>0.0005</td>
</tr>
<tr>
<td>UN(2, 1)</td>
<td>4.0708</td>
<td>11.8356</td>
<td>0.34</td>
<td>0.7309</td>
</tr>
<tr>
<td>UN(2, 2)</td>
<td>8.5480</td>
<td>6.6839</td>
<td>1.28</td>
<td>0.1005</td>
</tr>
<tr>
<td>UN(3, 1)</td>
<td>-1.8365</td>
<td>0.9877</td>
<td>-1.86</td>
<td>0.0630</td>
</tr>
<tr>
<td>UN(3, 2)</td>
<td>-0.5837</td>
<td>0.5927</td>
<td>-0.98</td>
<td>0.3247</td>
</tr>
<tr>
<td>UN(3, 3)</td>
<td>0.05677</td>
<td>0.05445</td>
<td>1.04</td>
<td>0.1486</td>
</tr>
</tbody>
</table>
Figure 2.1 Individual grow curves for some categories using model without interactions for treatments and other variables.
The fitted lines of Figure 2.1 were obtained using this model for different categories which are female in SES class 4 with radiation, male in SES class 4 with radiation, female in SES class 3 with chemotherapy, and male in SES class 3 with chemotherapy.

Interaction effects are an important consideration for any model and must be thoroughly explored to determine if there is a significant interaction that should be included in the model. Therefore, the interaction effects between variables are considered. Backward variable selection method was used to obtain the second model. The fixed effects of this model are showed in Table 2.4 and the variances of the intercepts and slopes are presented in Table 2.5. The fitted lines of Figure 2.2 were obtained using this model for different categories.

Table 2.4: Fixed effects for the model with interactions for treatments and other variables

| Effect          | Estimate | Error  | DF  | Pr > |t| |
|-----------------|----------|--------|-----|-------|---|
| Intercept       | 114.46   | 5.9135 | 46  | <.0001|
| SES             | -5.5096  | 1.4460 | 46  | 0.0004|
| genderf         | -2.4104  | 4.5038 | 46  | 0.5951|
| genderf*NPS_Ch  | 17.7229  | 7.3977 | 46  | 0.0207|
| time            | -10.1627 | 2.2317 | 379 | <.0001|
| time*NPS_Rad    | 8.6434   | 2.2625 | 379 | 0.0002|
| NPS_Ch          | -13.2480 | 5.0315 | 46  | 0.0115|
| NPS_Rad         | -0.8168  | 4.4896 | 46  | 0.8564|
Table 2.5: Random effects for the model with interactions for treatments and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Pr Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN(1,1)</td>
<td>168.49</td>
<td>46.6410</td>
<td>0.0002</td>
</tr>
<tr>
<td>UN(2,1)</td>
<td>-10.4186</td>
<td>5.5151</td>
<td>0.0589</td>
</tr>
<tr>
<td>UN(2,2)</td>
<td>1.3735</td>
<td>0.6981</td>
<td>0.0246</td>
</tr>
</tbody>
</table>

Female in SES class 4 with radiation

Male in SES class 4 with radiation
In the former two models, quadratic time was considered as a potential predictor. In the third model, fractional polynomial transformation was applied to continuous variables, SES, age at diagnosis, and time. For convenience, time was shifted two units before variable transformation. Table 2.6 shows the results of fractional polynomial transformation calculation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES</td>
<td>-0.5</td>
<td>-1</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>-0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Time</td>
<td>-2</td>
<td>-2</td>
</tr>
</tbody>
</table>
According to the results, the following transformations were applied before model building.

\[
sestr1 = SES^{-0.5}
\]

\[
sestr2 = \frac{1}{SES}
\]

\[
timetr1 = (time + 2)^{-2}
\]

\[
timetr2 = timetr1 \times \ln(time + 2)
\]

\[
agedxtr1 = (age_{dx})^{-0.5}
\]

\[
agedxtr2 = \sqrt{age_{dx}}
\]

After the variable transformation, every single variable was tested. Table 2.7 shows the results. Variable Surgery and Gender were not considered as potential predictors since their p-values were larger than 0.05.

Table 2.7: Results of testing the significance of variables

<table>
<thead>
<tr>
<th>Effect</th>
<th>NumDF</th>
<th>DenDF</th>
<th>FValue</th>
<th>ProbF</th>
</tr>
</thead>
<tbody>
<tr>
<td>sestr1</td>
<td>1</td>
<td>431</td>
<td>62.44301</td>
<td>2.31E-14</td>
</tr>
<tr>
<td>sestr2</td>
<td>1</td>
<td>431</td>
<td>55.3219</td>
<td>5.58E-13</td>
</tr>
<tr>
<td>agedxtr1</td>
<td>1</td>
<td>431</td>
<td>17.37366</td>
<td>3.71E-05</td>
</tr>
<tr>
<td>agedxtr2</td>
<td>1</td>
<td>431</td>
<td>39.77901</td>
<td>7.06E-10</td>
</tr>
<tr>
<td>genderf</td>
<td>1</td>
<td>431</td>
<td>1.405572</td>
<td>0.236446</td>
</tr>
<tr>
<td>timetr1</td>
<td>1</td>
<td>431</td>
<td>55.53379</td>
<td>5.07E-13</td>
</tr>
<tr>
<td>timetr2</td>
<td>1</td>
<td>431</td>
<td>60.94025</td>
<td>4.51E-14</td>
</tr>
<tr>
<td>NPS Ch</td>
<td>1</td>
<td>431</td>
<td>18.50414</td>
<td>2.1E-05</td>
</tr>
<tr>
<td>NPS Rad</td>
<td>1</td>
<td>431</td>
<td>23.96981</td>
<td>1.39E-06</td>
</tr>
<tr>
<td>Surgery</td>
<td>1</td>
<td>431</td>
<td>1.142278</td>
<td>0.28577</td>
</tr>
</tbody>
</table>
The fixed effects are showed in Table 2.8. Table 2.9 shows the random effects of the hierarchical model. The fitted lines of Figure 2.3 present individual growth curves for some categories.

Table 2.8: Fixed effects for the model with variable transformation for treatments and other variables

| Effect              | Estimate | Error     | DF   | Pr > |t| |
|---------------------|----------|-----------|------|-------|---|
| Intercept           | 83.9155  | 45.2855   | 88   | 0.0672  |
| sestr1              | -166.01  | 135.06    | 88   | 0.2223  |
| sestr1*timetr1      | -4025.36 | 1549.60   | 333  | 0.0098  |
| sestr1*timetr2      | 7745.86  | 2576.42   | 333  | 0.0028  |
| sestr2              | 144.94   | 94.9725   | 88   | 0.1306  |
| timetr1*sestr2      | 2817.46  | 1067.15   | 333  | 0.0087  |
| timetr2*sestr2      | 5436.34  | 1775.24   | 333  | 0.0024  |
| timetr1             | 1282.81  | 526.40    | 333  | 0.0153  |
| timetr2             | -2269.15 | 878.04    | 333  | 0.0102  |
| agedxtr2            | 6.4448   | 2.0919    | 88   | 0.0028  |
| timetr2*NPS_Rad     | -161.59  | 80.1186   | 333  | 0.0445  |
| NPS_Rad             | 25.3565  | 13.5932   | 88   | 0.0655  |

Table 2.9: Random effects for the model with variable transformation for treatments and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Pr Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>167.41</td>
<td>36.8730</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>timetr1</td>
<td>148.31</td>
<td>1444.61</td>
<td>0.4591</td>
</tr>
<tr>
<td>timetr2</td>
<td>4226.77</td>
<td>3544.09</td>
<td>0.1165</td>
</tr>
</tbody>
</table>
Figure 2.3 Individual growth curves for some categories using model with variable transformation for treatments and other variables.
The individual growth curves can be obtained based on these models for comparison. Figure 2.4 are individual growth curves for two patients.

Figure 2.4: Individual growth curves for treatments and other variables
2.3.2 Individual Growth Models for Neurological Predictor Scale and other variables

The variables interested are Years between date of treatment and date of exam (Time), Gender, Age group, SES classes, and Neurological Predictor Scale (NPS_total). The patients are divided into two age groups according to the age of diagnosis at cutting point seven-year-old. Based on Age group (0: age at diagnosis is less than 7 years old, 1: otherwise), Gender (1=Female, 0=Male), and SES class (1, 2, 3, 4, 5), 20 categories are defined.

Quadratic Time is considered as a potential predictor in the first two models in order to investigate the quadratic change in PPVT scores.

In the first model, only single terms are considered. The solution for fixed effects is presented in Table 2.10. The variables, quadratic time and gender, are not included since they don’t have significant effects on patients’ PPVT scores. Table 2.11 shows the random effects which are the variances of the intercept and linear slope.

Table 2.10: Fixed effects for the model without interaction effects for Neurological Predictor Scale and other variables

| Effect   | Estimate | Standard Error | DF  | Pr > |t| |
|----------|----------|----------------|-----|-------|-----|
| Intercept| 118.66   | 4.4628         | 16  | <.0001|   |
| SES      | -6.0842  | 1.0476         | 16  | <.0001|   |
| agegr    | 6.9888   | 2.6796         | 16  | 0.0190|   |
| time     | -1.7021  | 0.6394         | 412 | 0.0081|   |
| NPS_total| -1.4556  | 0.4969         | 412 | 0.0036|   |
Table 2.11: Random effects for the model without interaction effects for Neurological Predictor Scale and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Pr</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN(1, 1)</td>
<td>22.1920</td>
<td>15.8987</td>
<td>0.0814</td>
<td>0.0814</td>
</tr>
<tr>
<td>UN(2, 1)</td>
<td>-4.6762</td>
<td>5.1549</td>
<td>0.3643</td>
<td>0.3643</td>
</tr>
<tr>
<td>UN(2, 2)</td>
<td>3.9081</td>
<td>2.5472</td>
<td>0.0625</td>
<td>0.0625</td>
</tr>
</tbody>
</table>

The fitted lines of Figure 2.5 were obtained using this model for different categories which are female in ses class 4, male in ses class 4, children with 5 NPS_total, and children with 9 NPS_total.
In the second model, the interactions between variables are considered to investigate the change in patients’ PPVT. Table 2.12 shows the solution for fixed effects of this model and Table 2.13 shows the random effects. The fitted lines of Figure 2.6 were obtained using this model for different categories.
Table 2.12: Fixed effects for the model with interaction effects for Neurological Predictor Scale and other variables

| Effect          | Estimate | Error   | DF | Pr > |t| |
|-----------------|----------|---------|----|-------|---|
| Intercept       | 113.08   | 4.8967  | 14 | <.0001|   |
| SES             | -4.1534  | 1.2509  | 14 | 0.0051|   |
| SES*genderf     | -4.4570  | 2.0187  | 14 | 0.0444|   |
| agegr           | 5.4483   | 2.5270  | 14 | 0.0490|   |
| genderf         | 15.2616  | 6.6654  | 14 | 0.0381|   |
| time            | -1.7203  | 0.6244  | 412| 0.0061|   |
| NPS_total       | -1.4828  | 0.4973  | 412| 0.0030|   |

Table 2.13: Random effects for the model with interaction effects for Neurological Predictor Scale and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Pr Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN(1,1)</td>
<td>29.8876</td>
<td>21.1802</td>
<td>0.0791</td>
</tr>
<tr>
<td>UN(2,1)</td>
<td>-8.3105</td>
<td>6.4492</td>
<td>0.1975</td>
</tr>
<tr>
<td>UN(2,2)</td>
<td>3.8318</td>
<td>2.5418</td>
<td>0.0658</td>
</tr>
</tbody>
</table>
Figure 2.6 Individual grow curves for some categories using model with interactions for Neurological Predictor Scale and other variables
In the third model, quadratic time is not considered as a potential predictor. The fractional polynomial transformation is applied to determine the powers for continuous variables like SES, age at diagnosis, time and Neurological Predictor Scale (NPS_total). The following transformations were applied for these variables.

\[
\begin{align*}
sestr_1 &= \frac{1}{\sqrt{SE}} \\
sestr_2 &= \frac{1}{SE} \\
timetr_1 &= \frac{1}{(time + 2)^2} \\
timetr_2 &= timetr_1 \times \ln(time + 2) \\
agedxtr_1 &= \frac{1}{\sqrt{age - dx}} \\
agedxtr_2 &= \sqrt{age - dx} \\
totaltr_1 &= \frac{1}{NPS_{\text{total}}^2} \\
totaltr_2 &= \frac{1}{NPS_{\text{total}}}
\end{align*}
\]

The results of test for significance of the variables are showed in Table 2.14. Variable Surgery and Gender are not considered as potential predictors since their p-values are larger than 0.05.
Table 2.14: Results of testing the significance of Neurological Predictor Scale

<table>
<thead>
<tr>
<th>Effect</th>
<th>NumDF</th>
<th>DenDF</th>
<th>FValue</th>
<th>ProbF</th>
</tr>
</thead>
<tbody>
<tr>
<td>sestr1</td>
<td>1</td>
<td>431</td>
<td>62.44301</td>
<td>2.31E-14</td>
</tr>
<tr>
<td>sestr2</td>
<td>1</td>
<td>431</td>
<td>55.3219</td>
<td>5.58E-13</td>
</tr>
<tr>
<td>agedxtr1</td>
<td>1</td>
<td>431</td>
<td>17.37366</td>
<td>3.71E-05</td>
</tr>
<tr>
<td>agedxtr2</td>
<td>1</td>
<td>431</td>
<td>39.77901</td>
<td>7.06E-10</td>
</tr>
<tr>
<td>genderf</td>
<td>1</td>
<td>431</td>
<td>1.405572</td>
<td>0.236446</td>
</tr>
<tr>
<td>timetr1</td>
<td>1</td>
<td>431</td>
<td>55.53379</td>
<td>5.07E-13</td>
</tr>
<tr>
<td>timetr2</td>
<td>1</td>
<td>431</td>
<td>60.94025</td>
<td>4.51E-14</td>
</tr>
<tr>
<td>NPS_Ch</td>
<td>1</td>
<td>431</td>
<td>18.50414</td>
<td>2.1E-05</td>
</tr>
<tr>
<td>NPS_Rad</td>
<td>1</td>
<td>431</td>
<td>23.96981</td>
<td>1.39E-06</td>
</tr>
<tr>
<td>Surgery</td>
<td>1</td>
<td>431</td>
<td>1.142278</td>
<td>0.28577</td>
</tr>
<tr>
<td>totaltr1</td>
<td>1</td>
<td>431</td>
<td>4.268787</td>
<td>0.039416</td>
</tr>
<tr>
<td>totaltr2</td>
<td>1</td>
<td>431</td>
<td>16.51335</td>
<td>5.74E-05</td>
</tr>
</tbody>
</table>

The potential predictors, sestr1, sestr2, agedxtr1, agedxtr2, timetr1, timetr2, nps_ch, nps_rad, totaltr1, totaltr2 and their interactions are analyzed to build the model using PROC MIXED. Table 2.15 shows the fixed effects and Table 2.16 shows the random effects. The fitted lines in Figure 2.7 were obtained using this model.
Table 2.15: Fixed effects for the model with variable transformation for Neurological Predictor Scale and other variables

| Effect               | Estimate       | Error      | DF    | Pr > |t| |
|----------------------|----------------|------------|-------|-------|-----|
| Intercept            | 75.3855        | 47.5474    | 84    | 0.1166|
| sestr1               | -121.20        | 130.09     | 84    | 0.3542|
| sestr1*timetr1       | -4139.79       | 1542.20    | 334   | 0.0076|
| sestr1*timetr2       | 7973.02        | 2543.21    | 334   | 0.0019|
| sestr2               | 72.1730        | 93.5447    | 84    | 0.4426|
| sestr2*agedxtr2      | 18.5059        | 8.4949     | 84    | 0.0322|
| timetr1*sestr2       | 2923.85        | 1061.65    | 334   | 0.0062|
| timetr2*sestr2       | 2923.85        | 1061.65    | 334   | 0.0062|
| agedxtr1             | 32.6504        | 14.8082    | 84    | 0.0302|
| agedxtr1*totaltr1    | -1044.50       | 435.01     | 84    | 0.0186|
| agedxtr2             | -0.2725        | 6.0928     | 84    | 0.9644|
| timetr1              | 1308.22        | 524.23     | 334   | 0.0131|
| timetr2              | -2456.94       | 864.85     | 334   | 0.0048|
| totaltr1             | 153.06         | 261.13     | 84    | 0.5593|
| totaltr2             | 164.61         | 83.9317    | 84    | 0.0532|

Table 2.16: Random effects for the model with variable transformation for Neurological Predictor Scale and other variables

<table>
<thead>
<tr>
<th>Cov Parm</th>
<th>Estimate</th>
<th>Error</th>
<th>Pr</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>154.92</td>
<td>33.0145</td>
<td>&lt; .0001</td>
<td></td>
</tr>
<tr>
<td>timetr1</td>
<td>378.44</td>
<td>1300.80</td>
<td>0.3856</td>
<td></td>
</tr>
<tr>
<td>timetr2</td>
<td>2715.01</td>
<td>3056.25</td>
<td>0.1872</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2.7 Individual grow curves for some categories using model with variable transformation for Neurological Predictor Scale and other variables.
The individual growth curves can be obtained based on these models. Figure 2.8 are individual growth curves for two patients.

Figure 2.8: Individual growth curves for Neurological Predictor Scale and other variables
Chapter Three: Results and Discussion

In this chapter, the six individual growth models presented in previous chapter are discussed respectively and compared with each other.

3.1 Models for treatments and other variables

3.1.1 Model without interactions

Table 2.1 and Table 2.2 present the results of fitting this model. There is a significant mean PPVT difference due to ses class and age group. The average PPVT score at origin time is 103.1 for ses class1 and age less than 7 years old and is 111.8 for ses class 1 and age not less than 7 years old. For the same age group, the score decreases 5.6 as ses class increases one level. The coefficients of time and quadratic time indicate that the mean value decreases at 3.4 per year but the rate is slightly slow down (0.2 per quadratic year).

The estimated variance of intercepts and slopes is 126.26 (p=0.0005), 8.54 (p=0.1006) and 0.06 (p=0.1486) respectively. The significant intercept variance means that individuals vary in the level of PPVT score; the non-significant slope variances indicate that they don’t vary very much in rate and direction of change in PPVT score.

3.1.2 Model with interactions

The results of fitting this model are presented in Table 2.4 and Table 2.5. There is a significant interaction between gender and chemotherapy for mean PPVT difference. With other factors being equal, female with chemotherapy patients have
higher average PPVT score than that of male by 17.7. The main effects of radiation (p=0.8564) and gender (p=0.5961) are non-significant. The average PPVT score decreases while ses class increases one level with other factors unchanged. The PPVT will decrease significantly if chemotherapy is given. There is a significant difference in the rate of PPVT change across time where patients with radiation have a little bit higher score than the baseline mean PPVT. However, the rate of increase across time in PPVT score (10.2 per year) is driving it going down. The surgery and age at diagnosis are no longer significant effects in this model.

The estimated variance of intercept and slope is 168.49 (p=0.0002) and 1.3735 (p=0.0246) respectively. The significant intercept variance means that individuals vary in the level of PPVT score; the significant slope variance indicates that they vary in rate and direction of change in PPVT score.

### 3.1.3 Model with variable transformation

Compared with the other two models, this model is complicated. Table 2.8 and Table 2.9 present the results of fixed effects and random effects. The rate of increase across time in PPVT score is non-linear. Table 3.1 presents some fit statistics of these three models.
Table 3.1: Comparison of models for treatments and other variables

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Model without interactions</th>
<th>Model with interactions</th>
<th>Model with variable transformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 Res Log Likelihood</td>
<td>3539.9</td>
<td>3512.0</td>
<td>3157.9</td>
</tr>
<tr>
<td>AIC (the smaller the better)</td>
<td>3553.9</td>
<td>3520.0</td>
<td>3165.9</td>
</tr>
<tr>
<td>AICC (the smaller the better)</td>
<td>3554.2</td>
<td>3520.1</td>
<td>3166.0</td>
</tr>
<tr>
<td>BIC (the smaller the better)</td>
<td>3567.6</td>
<td>3527.8</td>
<td>3176.1</td>
</tr>
</tbody>
</table>

3.2 Models for Neurological Predictor Scale and other variables

3.2.1 Model without interactions

Table 2.10 and Table 2.11 present the results of fitting this model. There is a significant mean PPVT difference due to ses class, age group and Neurological Predictor Scale. The average PPVT score at origin time is 112.5 for ses class 1, age less than 7 years old and no treatments and is 119.5 for ses class 1, age not less than 7 years old and no treatment. For the same age group with no treatment, the mean score decreases 6.1 as ses class increases one level. The higher level of total Neurological Predictor Scale has lower mean PPVT. The rate of increase in PPVT is driving the mean value decreasing at 1.7 point per year.

The estimated variance of intercept and slope is 22.1920 (p=0.0814) and 3.9081 (p=0.0625) respectively. The non-significant intercept variance means that individuals vary not much in the level of PPVT score; the significant slope variance indicates that they vary in rate and direction of change in PPVT score.
3.2.2 Model with interactions

Table 2.12 and Table 2.13 show the results of fitting this model. There is a significant interaction between gender and ses class for mean PPVT difference. With other factors being equal, female in ses class 1 patients have lower average PPVT score than that of male by 4.5. There is significance due to the main effects of the total number of treatment (p=0.003) where the average PPVT for subjects without treatment is 113.1 and is 111.6 for patients taking only 1 treatment with other factors being equal. The average PPVT score decreases while ses class increases one level with other factors unchanged. The mean PPVT will increase significantly if age at diagnosis increases. The rate of increase across time in PPVT score (1.7 point per year) is driving it going down.

The estimated variance of intercept and slope is 29.89 (p=0.08) and 3.8 (p=0.07) respectively. The non-significant intercept variance means that individuals vary not much in the level of PPVT score; the non-significant slope variance indicates that they vary not significantly in rate and direction of change in PPVT score.

3.2.3 Model with variable transformation

Table 2.15 and Table 2.16 present the results of fixed effects and random effects for this model. The rate of increase across time in mean PPVT score is non-linear. The variables ses class, age at diagnosis and Neurological Predictor Scale have complicated significant effects of change in PPVT. However, gender is no longer a significant effect in this model. Table 3.2 presents some fit statistics of these three models.
Table 3.2: Comparison of models for Neurological Predictor Scale and other variables

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Model without interactions</th>
<th>Model with interactions</th>
<th>Model with variable transformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 Res Log Likelihood</td>
<td>3537.2</td>
<td>3523.6</td>
<td>3114.3</td>
</tr>
<tr>
<td>AIC (the smaller the better)</td>
<td>3545.2</td>
<td>3531.6</td>
<td>3122.3</td>
</tr>
<tr>
<td>AICC (the smaller the better)</td>
<td>3545.3</td>
<td>3531.7</td>
<td>3122.4</td>
</tr>
<tr>
<td>BIC (the smaller the better)</td>
<td>3553.0</td>
<td>3539.4</td>
<td>3132.5</td>
</tr>
</tbody>
</table>
Chapter Four: Conclusion and Future Research

It has been shown in the literature on the developmental late-effects of radiation therapy that the increased survival rate is associated with the risk of suboptimal behavior, emotional, and cognitive outcomes [4, 11].

In this study, the analyses using individual growth models show a linear decline in average PPVT score over time. The quadratic rate, however, is not clear for this data set. Different treatment shows different effect on the change in PPVT. In this study, surgery shows the least effect, the chemotherapy tends to let the average PPVT score go down, and radiation therapy tends to accelerate the change rate. The average score decreases as Neurological Predictor Scale increases. The age at diagnosis also affects the score. The patients at diagnostic age older than 7 years old tend to have higher score than that of people at age less than 7 years old.

The individual growth model in modeling longitudinal change has been applied to many research fields. This study highlights the usefulness of this method in modeling change in children’s learning and memory variables.

Since only 45 patients (about 40% of the sample) have more than 2 measurements, a larger sample size is needed for more sophisticated statistical analyses and greater statistical power. For example, the quadratic rate of change may be addressed and more accurate trajectories of the scores can be studied.
References


[5] Department of Psychology, Georgia State University 
http://www2.gsu.edu/~wwwpsy/faculty/king.htm/.


Appendix A: SAS Code

Libname A 'C:\Documents and Settings\yinshen\My Documents\Thesis\DX';
/* Merge BTPPVT_NPS_TREATMENT and yusheng_tmt_PPVT_test.xls to generate the total study cohort */

proc import datafile='C:\Documents and Settings\yinshen\My Documents\Thesis\DX\yusheng_tmt_PPVT_test.xls' out=test dbms=excel replace;run;

proc sort data=a.btppvt_nps_treatment out=treatment; by idnum;run;
proc sort data=test(rename=(id_number=idnum)) out=test; by idnum;run;

data character;
    set test;
    if idnum;
    age_dx=yrdif(DOB, Date_of_Dx_, 'ACT/ACT');run;

data a.total;
    merge treatment character;
    by idnum;
    if idnum;
    if NPS_Rad=2 or NPS_Rad=3 then NPS_Rad=1;
    time=yrdif(Date_of_Dx_, dateppvt,'ACT/ACT');
run;

data a.cohort;
    set a.total(keep=idnum dob dateppvt ppvtss ses gender Date_of_Dx_ surgery nps_rad nps_ch nps_total age_dx time);
    genderf=0; if gender='F' then genderf=1;
    sur='w/o';if surgery=1 then sur='W';
    ch='w/o';if nps_ch=1 then ch='W';
    rad='w/o';if nps_rad=1 then rad='W';
    time2=time+2;
    time_sq=time**2;
    if ses=. then delete;
    if ppvtss=. then delete;
    if age_dx<0 then delete; *id=226;
    p1=-2;p2=-1;p3=-0.5;p4=0;p5=0.5;p6=1;p7=2;p8=3;
run;

proc export data=a.cohort
    outfile='C:\Documents and Settings\yinshen\My Documents\Thesis\DX\BZ1024.xls'
    dbms=excel replace;
run;

/****Profile Plots****/
goption reset=all;
symbol interpol=join repeat=300 ;
proc gplot data=a.cohort;
    plot ppvtss* time=idnum;
run;quit;
/*** Fractional Polynomial Transformation ***/
*ods trace on/listing label;
ods trace off;

%macro fractional(res, var);
data out1factor out2factor;
   if 1=1 then delete;
run;
%do n=1 %to 8;
data sample&n;
   set a.cohort;
   if p&n=0 then u1=log(&var);else u1=&var**p&n;
run;
ods output Mixed.FitStatistics=out&n;
proc mixed data=sample&n;
   class genderf NPS_Rad NPS_Ch surgery;
   model &res=u1;
   run;

data out&n;
   merge out&n(obs=1) a.cohort(obs=1);
   f1=p&n;D=Value;
   keep f1 D;
run;
data out1factor;
   set out1factor out&n;
run;
%do m=1 %to 8;
data sample&n&m;
   set a.cohort;
   if p&n=0 then u1=log(&var);else u1=&var**p&n;
   if p&m=p&n then u2=log(&var)*u1;else if p&m=0 then
      u2=log(&var);else u2=&var**p&m;
run;
ods output Mixed.FitStatistics=out&n&m;
proc mixed data=sample&n&m ;
   class genderf NPS_Rad NPS_Ch surgery;
   model &res=u1 u2;
   run;

data out&n&m;
   merge out&n&m(obs=1) a.cohort(obs=1);
   f1=p&n;f2=p&m;D=Value;
   keep f1 f2 D;
run;
data out2factor;
   set out2factor out&n&m;
run;
%end;
%end;

proc iml;
   use out1factor;
   read all var{f1 D} into model1;
close out1factor;
L1=model1[1,1]; P1=model1[1,1];
nrow1=nrow(model1);
do i=2 to nrow1;
   if model1[i,1]=1 then L=model1[i,2];
   if model1[i,2]<L1 then do;
      L1=model1[i,2];P1=model1[i,1];
   end;
end;
use out2factor;
read all var{f1 f2  D} into model2;
close out2factor;
L2=model2[1,1]; P21=model2[1,1];P22=model2[1,2];
nrow2=nrow(model2);
do i=2 to nrow2;
   if model2[i,3]<L2 then do;
      L2=model2[i,3];P21=model2[i,1];P22=model2[i,2];
   end;
end;
if L-L1>3.84 then do; /*chi-sq(.95,1)=3.84; chi-
   sq(.95,2)=5.99; chi-sq(.95,3)=7.81;*/
   if L1-L2>5.99 then print 'the best is model2 with
      power' P21 'and' P22;
   else print 'the best is model1 with power' P1;
   end;
else do;
   if L-L2>7.81 then print 'the best is model2 with power' P21
      'and' P22;
   else print 'the best is linear model' ;
end;
quit;
%mend fractional;
%fractional (ppvtss, time);
%fractional (ppvtss, time2);
%fractional (ppvtss, ses);
%fractional (ppvtss, age_dx);
%fractional (ppvtss, nps_total);
data three;
   set a.cohort;
   sestr1=ses**(-0.5);sestr2=ses**(-1);
   /* timetr1=time2**(-0.5);timetr2=time2**(-1); */
   agedxtr1=age_dx**(-0.5);agedxtr2=age_dx**0.5;
   totaltr1=NPS_Total**(-2);totaltr2=NPS_Total**(-1);
run;

*Variable:  SES Age_dx genderf time time_sq NPS_Ch NPS_Rad Surgery;
*GROUP patients by Nps-Rad Nps_Ch Surgery Genderf Ses agegr, typically
sub=160;
data one;
   set a.cohort;
   if ses=. then delete;
   if ppvtss=. then delete;
   if age_dx gt 7 then agegr=1; else agegr=0;
   if Nps_Rad=0 then sub=1;else sub=2;
if Nps_Ch=1 then sub=sub+2;
if Surgery=1 then sub=sub+4;
if genderf=1 then sub=sub+8;
do i=1 to 5;
    if ses=i then sub=sub+16*(i-1);
end;
if agegr=1 then sub=sub+80;
run;
proc sort data=one out=two;by sub;run;

*model without interactions;
proc mixed data=two covtest;
    class idnum sub sur gender ch rad;
    model ppvtss=time time_sq ses agegr gender sur rad ch/s;
run;
proc mixed data=two covtest;
    class idnum sub sur gender ch rad;
    model ppvtss=time ses agegr ch/s;
run;
proc mixed data=two covtest;
    class idnum sub sur gender ch rad;
    model ppvtss=time ses agegr ch/s;
    random intercept time/s sub=sub type=un;
run;
*ods trace on;
ods trace off;
ods output Mixed.SolutionR=mixs;
ods output Mixed.SolutionF=fixs;
proc mixed data=two covtest;
    class idnum sub sur gender ch rad;
    model ppvtss=time ses agegr ch/s;
    random intercept time/s sub=sub type=un;
run;
proc transpose data=mixs out=mix;
    by sub;
    var estimate;
    id effect;
    run;
data fixs;
set fixs;
if estimate=0 then delete;
run;
proc transpose data=fixs out=fix;
    var estimate;
    id effect;
    run;
data fix;
    set fix(drop=_name_ rename=(intercept=fint time=ft ses=fses ch=fch));
do i=1 to 433;
output;
end;
drop i;
run;
data test1;
merge two fix;
run;
data test2;
merge test1 mix(drop=_name_ rename=(intercept=rint time=rt ));
by sub;
run;
data test3;
set test2;
exp_ppvtss=(fint+rint)+(ft+rt)*time+fses*ses+fch*nps_ch;
run;
data m11;
set test3(rename=(exp_ppvtss=exp_ppvtss1));run;
data ses1 ses2 ses3 ses4 ses5;
set test3;
   if ses=1 then output ses1;
   else if ses=2 then output ses2;
   else if ses=3 then output ses3;
   else if ses=4 then output ses4;
   else output ses5;
run;
data ses4radf ses4radm;
set ses4;
   if Nps_Rad=1 & genderf=1 then output ses4radf;
   if Nps_Rad=1 & genderf=0 then output ses4radm;
run;
data ses3chf ses3chm;
set ses3;
   if Nps_ch=1 & genderf=1 then output ses3chf;
   if Nps_ch=1 & genderf=0 then output ses3chm;
run;
goption reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);
proc gplot data=ses4radf;
title 'Female in SES class 4 with radiation';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses4radm;
title 'Male in SES class 4 with radiation';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses3chf;
title 'Female in SES class 3 with chemotherapy';
plot exp ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=ses3chm;
title 'Male in SES class 3 with chemotherapy';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=ses4;
plot (exp_ppvtss ppvtss)*time=idnum/vaxis = axis1;
run;quit;

*model with interactions;
%macro mix_inter(res, var1, var2, var3, var4, var5, var6, var7, var8);
proc mixed data=two;
class idnum sub sur ch rad gender;
%let reg=;
%let item=;
%do i=1 %to 7;
	%let it=&&var&i;
	%do j=&i+1 %to 8;
		%let item=&&item &it &var&i*&&var&j;
%end;
%let reg=&reg &it &item;
%let item=;
%if &i=7 %then %let reg=&reg &var8;
%end;
model &res=&reg ;
run;
%mend mix_inter;
%mix_inter(ppvtss, ses, agegr, gender, time, time_sq, Ch, Rad, sur);

proc mixed data=two covtest;
class idnum sub sur ch rad gender;
model ppvtss=SES SES*Gender SES*time SES*time_sq SES*sur agegr agegr*time_sq agegr*ch agegr*rad agegr*sur Gender time*Gender time_sq*Gender ch*Gender rad*Gender sur*Gender time time_sq time*rad time_sq time_sq*rad ch ch*rad sur*ch rad sur*rad sur ;
run;
proc mixed data=two covtest;
class idnum sub sur ch rad gender;
model ppvtss=SES SES*Gender agegr agegr*rad agegr*sur Gender time*Gender ch*Gender rad*Gender time time_sq time_sq*rad ch sur*ch rad sur ;
run;
proc mixed data=two covtest;
class idnum sub sur ch rad gender;
model ppvtss=SES SES*Gender agegr
agegr*rad  agegr*sur  Gender  time*Gender ch*Gender rad*Gender
time  time*rad  time_sq  time_sq*rad  ch
sur*ch  rad  sur  /s;
random intercept time time_sq/s  type=un  sub=idnum;
run;
ods output  Mixed.SolutionR=mixs;
ods output  Mixed.SolutionF=fixs;
proc mixed data=two covtest;
class idnum sub sur ch rad gender;
model ppvtss=SES Gender  time*Gender ch*Gender rad*Gender
time  time*rad  time_sq  time_sq*rad rad ch /s;
random intercept time time_sq/s  type=un  sub=idnum;
run;
proc transpose data=mixs out=mix;
   by idnum;
      var estimate;
      id effect;
run;
data fixes;
set fixes;
if estimate=0 then delete;
if effect='time*Gender' and gender='F' then effect='timef';
if effect='time*Gender' and gender='M' then effect='timem';
if effect='ch*Gender' and gender='F' then effect='chf';
if effect='ch*Gender' and gender='M' then effect='chm';
if effect='rad*Gender' and gender='F' then effect='radf';
if effect='rad*Gender' and gender='M' then effect='radm';
run;
proc transpose data=fixs out=fix;
   var estimate;
   id effect;
run;
data fix;
   set fix(drop=_name_ rename=(intercept=fint ses=fses gender=fgen
timef=ftimef
timem=ftimem chf=fchf chm=fchm radf=fradf radm=fadm
time_rad=ftimerad
time_sq=ftimesq time_sq_rad=ftimesqrad));
do i=1 to 433;
   output;
end;
drop i;
run;
data test1;
   merge two fix;
   run;
proc sort data=test1;
   by idnum;
run;
data test2;
**merge** test1 mix(drop=_name_ rename=(intercept=rint time=rt time_sq=rtsq));
by idnum;
run;

**data** test3;
set test2;
if gender='F' then
exp_ppvtss=(fint+rint)+fses*ses+fgen+(ftimef+rt)*time+fchf*nps_ch+frad
f*nps_rad
+ftimerad*time*nps_rad+(ftimesq+rtsq)*time_sq+ftimesqrad*time_sq*nps_rad;
else
exp_ppvtss=(fint+rint)+fses*ses+(ftimem+rt)*time+fchm*nps_ch+fradm*nps_rad
+ftimerad*time*nps_rad+(ftimesq+rtsq)*time_sq+ftimesqrad*time_sq*nps_rad;
run;

**data** m12;
set test3(rename=(exp_ppvtss=exp_ppvtss2));run;

**data** ses1 ses2 ses3 ses4 ses5;
set test3;
if ses=1 then output ses1;
else if ses=2 then output ses2;
else if ses=3 then output ses3;
else if ses=4 then output ses4;
else output ses5;
run;

**data** ses4radf ses4radm;
set ses4;
if Nps_Rad=1 & genderf=1 then output ses4radf;
if Nps_Rad=1 & genderf=0 then output ses4radm;
run;

**data** ses3chf ses3chm;
set ses3;
if Nps_ch=1 & genderf=1 then output ses3chf;
if Nps_ch=1 & genderf=0 then output ses3chm;
run;

goption reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);

**proc** gplot data=ses4radf;
title 'Female in SES class 4 with radiation';
plot exp ppvtss *time=idnum/ vaxis = axis1;
run;quit;
**proc** gplot data=ses4radm;
title 'Male in SES class 4 with radiation';
plot exp ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=ses3chf;
title 'Female in SES class 3 with chemotherapy';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=ses3chm;
title 'Male in SES class 3 with chemotherapy';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=female;
plot (exp_ppvtss ppvtss)*time=idnum/ vaxis = axis1;
run;

*model with variable transformation;

proc mixed data=three covtest;
class idnum ch rad sur gender;
model ppvtss=sestr1 sestr1*sestr2 sestr1*time sestr1*gender
      sestr1*agedxtr1 sestr1*agedxtr2 sestr1*sur sestr1*ch sestr1*rad
            sestr2 sestr2*time sestr2*gender sestr2*sestr2*agedxtr1
            sestr2*agedxtr2 sestr2*sur sestr2*ch sestr2*rad
            time*sur time*ch time*rad gender gender*agedxtr1 gender*agedxtr2 gender*sur
gender*ch gender*rad agedxtr1 agedxtr1*agedxtr2 agedxtr1*sur agedxtr1*ch
            agedxtr1*rad agedxtr2 agedxtr2*sur agedxtr2*ch agedxtr2*rad
            sur sur*ch sur*rad ch*rad rad;
run;
proc mixed data=three covtest;
class idnum ch rad sur gender;
model ppvtss=sestr1 sestr1*sestr2 sestr1*time sestr1*gender
      sestr1*agedxtr2 sestr1*rad
            sestr2 sestr2*time sestr2*agedxtr2 sestr2*rad
            time*genenr time*rad gender gender*ch gender*rad
            agedxtr1 agedxtr1*ch
            agedxtr2 agedxtr2*rad
            sur ch rad/s;
random intercept time/s sub=idnum type=un;
run;

ods output Mixed.SolutionR=mixs;
ods output Mixed.SolutionF=fixs;
proc mixed data=three covtest;
class idnum ch rad sur gender;
model ppvtss=sestr1
      time time*gender time*rad gender gender*ch gender*rad
            agedxtr2 agedxtr2*rad
            ch rad/s;
random intercept time/s sub=idnum type=un;
run;
proc transpose data=mixs out=mix;
   by idnum;
   var estimate;
   id effect;
run;
data fixes;
set fixes;
if estimate=0 then delete;
if effect='time*Gender' and gender='F' then effect='timef';
if effect='time*Gender' and gender='M' then effect='timem';
if effect='ch*Gender' and gender='F' then effect='chf';
if effect='ch*Gender' and gender='M' then effect='chm';
if effect='rad*Gender' and gender='F' then effect='radf';
if effect='rad*Gender' and gender='M' then effect='radm';
run;
proc transpose data=fixs out=fix;
   var estimate;
   id effect;
run;
data fixs;
set fixs;
   drop _name_; rename (intercept=fint sestr1=fses1
time=ftime timef=ftimef
   time_rad=ftimerad gender=fgen chf=fchf chm=fchm radf=fradf
   radm=fradm
   agedxtr2=fage2 agedxtr2_rad=fage2rad));
do i=1 to 433;
output;
end;
run;
data test1;
merge three fix;
run;
data test2;
merge test1 mix(drop=_name_ rename=(intercept=rint time=rt ));
by idnum;
run;
data test3;
set test2;
   if gender='F' then
   exp_ppvtss=(fint+rint)+fses1*sestr1+(ftime+rt+ftimef)*time+ftimerad*time
   +fchf*nps_ch+fradf*nps_rad+fage2*agedxtr2+fage2rad*agedxtr2*nps_rad;
else
   exp_ppvtss=(fint+rint)+fses1*sestr1+(ftime+rt)*time+ftimerad*time*nps_rad
   +fchm*nps_ch+fradm*nps_rad+fage2*agedxtr2+fage2rad*agedxtr2*nps_rad;
run;
```sas
data m13;
   set test3(rename=(exp_ppvtss=exp_ppvtss3));run;

data ses1 ses2 ses3 ses4 ses5;
   set test3;
      if ses=1 then output ses1;
      else if ses=2 then output ses2;
      else if ses=3 then output ses3;
      else if ses=4 then output ses4;
      else output ses5;
run;

data ses4radf ses4radm;
   set ses4;
      if Nps_Rad=1 & genderf=1 then output ses4radf;
      if Nps_Rad=1 & genderf=0 then output ses4radm;
run;

data ses3chf ses3chm;
   set ses3;
      if Nps_ch=1 & genderf=1 then output ses3chf;
      if Nps_ch=1 & genderf=0 then output ses3chm;
run;

option reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);
proc gplot data=ses4radf;
   title 'Female in SES class 4 with radiation';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses4radm;
   title 'Male in SES class 4 with radiation';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses3chf;
   title 'Female in SES class 3 with chemotherapy';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses3chm;
   title 'Male in SES class 3 with chemotherapy';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=female;
   plot (exp_ppvtss ppvtss)*time=idnum/ vaxis = axis1;
run;quit;
proc sort data=m11;
   by idnum time;
proc sort data=m12;
   by idnum time;
run;

data nps;
```
merge m11(keep=idnum ppvtss time Exp_ppvtss1) m12(keep=idnum Exp_ppvtss2)
 m13(keep=idnum Exp_ppvtss3);
by idnum;
run;
proc export data=nps
outfile='C:\Documents and Settings\yinshen\My Documents\Thesis\DX\NPS.xls'
dbms=excel
replace;
run;
/*******
/*Variable:  SES Age_dx genderf time time_sq NPS_total;*/
*GROUP;
data one;
set a.cohort;
if age_dx gt 7 then agegr=1; else agegr=0;
if genderf=0 then sub=1;else sub=2;
if agegr=1 then sub=sub+2;
do i=1 to 5;
  if ses=i then sub=sub+4*(i-1);
end;
run;
proc sort data=one out=two;by sub;run;
*model without interactions;
proc mixed data=two covtest;
class idnum sub gender;
model ppvtss=SES Agegr time time_sq gender NPS_total;
run;
proc mixed data=two covtest;
class idnum sub gender;
model ppvtss=SES Agegr time NPS_total/s;
run;
proc mixed data=two covtest;
class idnum sub gender;
model ppvtss=SES Agegr NPS_total/s;
random intercept time /s sub=sub  type=un;
run;
ods output Mixed.SolutionR=mixs;
ods output Mixed.SolutionF=fixs;
proc mixed data=two covtest;
class idnum sub gender;
model ppvtss=SES Agegr NPS_total/s;
random intercept /s sub=sub  type=un;
run;
proc transpose data=mixs out=mix;
by sub;
var estimate;
id effect;
run;

proc transpose data=fixs out=fix;
  var estimate;
  id effect;
run;

data fix;
  set fix(drop=_name_ rename=(intercept=fint ses=fses agegr=fage nps_total=ftotal));
  do i=1 to 433;
    output;
  end;
  drop i;
run;

data test1;
  merge two fix;
run;

data test2;
  merge test1 mix(drop=_name_ rename=(intercept=rint));
  by sub;
run;

data test3;
  set test2;
  exp_ppvtss=(fint+rint)+fses*ses+fage*agegr+ftotal*nps_total;
run;

data m21;
  set test3 (rename=(exp_ppvtss=exp_ppvtss1));run;

data ses1 ses2 ses3 ses4 ses5;
  set test3;
  if ses=1 then output ses1;
  else if ses=2 then output ses2;
  else if ses=3 then output ses3;
  else if ses=4 then output ses4;
  else output ses5;
run;

data ses4f ses4m;
  set ses4;
  if genderf=1 then output ses4f;
  else output ses4m;
run;

data total5 total9;
  set test3;
  if Nps_total=5 then output total5;
  if Nps_total=9 then output total9;
run;

goption reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);

proc gplot data=ses4f;
title 'Female in SES class 4';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=ses4m;
   title 'Male in SES class 4';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=total5;
   title 'Children with 5 total treatments';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

proc gplot data=total9;
   title 'Children with 9 total treatments';
   plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

*model with interactions;

proc mixed data=two covtest;
   class idnum sub gender;
   model ppvtss=SES ses*agegr ses*time ses*time_sq ses*gender
         ses*nps_total
         Agegr agegr*time agegr*time_sq agegr*gender
         agegr*nps_total
         time time*time_sq time*gender time*time_sq time*time_sq*gender time*nps_total
         gender gender*nps_total nps_total NPS_total;
run;

proc mixed data=two covtest;
   class idnum sub gender;
   model ppvtss=SES ses*time_sq ses*gender
         Agegr agegr*nps_total time_sq gender NPS_total;
run;

proc mixed data=two covtest;
   class idnum sub gender;
   model ppvtss=SES ses*time_sq ses*gender
         Agegr agegr*nps_total time_sq gender NPS_total/s;
   random intercept time_sq/s sub=sub type=un;
run;

proc mixed data=two covtest;
   class idnum sub gender;
   model ppvtss=SES ses*gender
         Agegr time_sq gender NPS_total/s;
   random intercept/time_sq/s sub=sub type=un;
run;
ods output Mixed.SolutionR=mixs;
ods output Mixed.SolutionF=fixs;
proc mixed data=two covtest;
   class idnum sub gender;
   model ppvtss=SES ses*gender
         Agegr gender NPS_total/s;
   random intercept/s sub=sub type=un;
run;

proc transpose data=mixs out=mix;
  by sub;
  var estimate;
  id effect;
run;

data fixs;
set fixs;
if estimate=0 then delete;
run;
proc transpose data=fixs out=fix;
  var estimate;
  id effect;
run;
data fix;
  set fix(drop=_name_ rename=(intercept=fint ses=fses
ses_gender=fsesgen agegr=fage
gender=fgen nps_total=ftotal));
  do i=1 to 433;
  output;
  end;
  drop i;
run;
data test1;
  merge two fix;
run;
data test2;
  merge test1 mix(drop=_name_ rename=(intercept=rint ));
  by sub;
run;
data test3;
  set test2;
  exp_ppvtss=(fint+rint)+fses*ses+fsesgen*ses*genderf+agegr+fgen*genderf+ftotal*nps_total;
run;
data m22;
  set test3 (rename=(exp_ppvtss=exp_ppvtss2));run;
data ses1 ses2 ses3 ses4 ses5;
set test3;
  if ses=1 then output ses1;
  else if ses=2 then output ses2;
  else if ses=3 then output ses3;
  else if ses=4 then output ses4;
  else output ses5;
run;
data ses4f ses4m;
set ses4;
  if genderf=1 then output ses4f;
  else output ses4m;
run;
data total5 total9;
  set test3;
  if Nps_total=5 then output total5;
  if Nps_total=9 then output total9;
run;

gooption reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);

proc gplot data=ses4f;
title 'Female in SES class 4';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses4m;
title 'Male in SES class 4';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=total5;
title 'Children with 5 total treatments';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=total9;
title 'Children with 9 total treatments';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;

*model with variable transformation;

proc mixed data=three covtest;
class idnum gender;
model ppvtss=sestr1 sestr1*sestr2 sestr1*time sestr1*gender sestr1*agedxtr1 sestr1*agedxtr2 sestr1*totaltr1 sestr1*totaltr2 sestr2 sestr2*time sestr2*gender sestr2*agedxtr1 sestr2*agedxtr2 sestr2*totaltr1 sestr2*totaltr2 time time*gender time*agedxtr1 time*agedxtr2 time*totaltr1 time*totaltr2 gender gender*agedxtr1 gender*agedxtr2 gender*totaltr1 gender*totaltr2 agedxtr1 agedxtr1*agedxtr2 agedxtr1*totaltr1 agedxtr1*totaltr2 agedxtr2 agedxtr2*totaltr1 agedxtr2*totaltr2 totaltr1 totaltr1*totaltr2 totaltr2;
run;
proc mixed data=three covtest;
class idnum gender;
model ppvtss=sestr1 sestr1*sestr2 sestr1*time sestr1*gender sestr1*agedxtr1 sestr1*agedxtr2 sestr2 sestr2*time sestr2*gender sestr2*agedxtr1 sestr2*agedxtr2 sestr2*totaltr1 sestr2*totaltr2 time time*gender time*totaltr2 gender gender*agedxtr1 gender*agedxtr2 gender*totaltr1 gender*totaltr2 agedxtr1 agedxtr1*agedxtr2 agedxtr1*totaltr1 agedxtr1*totaltr2 agedxtr2 agedxtr2*totaltr1 agedxtr2*totaltr2 totaltr1 totaltr1*totaltr2 totaltr2;
random intercept time /s sub=idnum type=un;
run;

proc mixed data=three covtest;
class idnum gender;
model ppvtss=sestr1 sestr1*gender time gender agedxtr1 agedxtr1*totaltr1 totaltr1 totaltr2/s;
random intercept time /s sub=idnum type=un;
run;
ods output Mixed.SolutionR=mixs;
ods output Mixed.SolutionF=fixs;
proc mixed data=three covtest;
class idnum gender;
model ppvtss=sestr1 sestr1*gender gender agedxtr1 agedxtr1*totaltr1 totaltr1 totaltr2/s;
random intercept/s sub=idnum type=un;
run;
proc transpose data=mixs out=mix;
   by idnum;
      var estimate;
      id effect;
   run;
data fixs;
set fixs;
if estimate=0 then delete;
run;
proc transpose data=fixs out=fix;
   var estimate;
   id effect;
   run;
data fix;
   set fix(drop=_name_ rename=(intercept=fint sestr1=fses1 sestr1_gender=fses1gen gender=fgen agedxtr1=fage1 agedxtr1_totaltr1=fage1total1 totaltr1=ftotal1 totaltr2=ftotal2));
do i=1 to 433;
output;
end;
drop i;
run;
data test1;
   merge three fix;
run;
data test2;
   merge test1 mix(drop=_name_ rename=(intercept=rint ));
   by idnum;
run;
data test3;
   set test2;
   exp_ppvtss=(fint+rint)+fses1*sestr1+fses1gen*sestr1*gender
+fgen*gender+fagel*agedxtrl+fageltotal1*agedxtrl*totaltr1+ftotal1*totaltr1+ftotal2*totaltr2

run;
data m23;
set test3(rename=(exp_ppvtss=exp_ppvtss3));run;
data ses1 ses2 ses3 ses4 ses5;
set test3;
if ses=1 then output ses1;
else if ses=2 then output ses2;
else if ses=3 then output ses3;
else if ses=4 then output ses4;
else output ses5;
run;
data ses4f ses4m;
set ses4;
if genderf=1 then output ses4f;
else output ses4m;
run;
data total5 total9;
set test3;
if Nps_total=5 then output total5;
if Nps_total=9 then output total9;
run;
gooption reset=all;
symbol interpol=join repeat=300;
axis1 label = (a=90);
proc gplot data=ses4f;
title 'Female in SES class 4';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=ses4m;
title 'Male in SES class 4';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=total5;
title 'Children with 5 total treatments';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc gplot data=total9;
title 'Children with 9 total treatments';
plot exp_ppvtss *time=idnum/ vaxis = axis1;
run;quit;
proc sort data=m21;
by idnum time;
proc sort data=m22;
by idnum time;
run;
data npstotal;
merge m21(keep=idnum ppvtss time Exp_ppvtss1) m22(keep=idnum
Exp_ppvtss2)
    m23(keep=idnum Exp_ppvtss3);
by idnum;
run;
proc export data=npstotal
    outfile='C:\Documents and Settings\yinshen\My
Documents\Thesis\DX\NPStotal.xls'
    dbms=excel
    replace;
run;
Appendix B: Models for time beginning from diagnosis date

Individual Growth Models for Treatments and other variables

Model without interaction

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num</th>
<th>Den</th>
<th>F Value</th>
<th>Pr &gt; F</th>
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</thead>
<tbody>
<tr>
<td>time</td>
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<td>47</td>
<td>7.54</td>
<td>0.0085</td>
</tr>
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<td>SES</td>
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<td>333</td>
<td>20.96</td>
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<tr>
<td>ch</td>
<td>1</td>
<td>333</td>
<td>4.78</td>
<td>0.0295</td>
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</table>

Fixed effects

| Effect | ch | Estimate | Standard Error | DF | t Value | Pr > |t| |
|--------|----|----------|----------------|----|---------|------|---|
| Intercept | ch | 116.14   | 5.2092         | 49 | 22.29   | <.0001 |
| Time    |    | -0.9632  | 0.3507         | 47 | -2.75   | 0.0085 |
| SES     |    | -6.4373  | 1.4059         | 333| -4.58   | <.0001 |
| ch      | W  | -8.0645  | 3.6886         | 333| -2.19   | 0.0295 |
| ch      | w/o| 0        | .              | .  | .       | .    |

Female in SES class 4 with radiation

![Graph showing female in SES class 4 with radiation](image-url)
Model with interactions

<table>
<thead>
<tr>
<th>Effect</th>
<th>Num</th>
<th>Den</th>
<th>F Value</th>
<th>Pr &gt; F</th>
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<tbody>
<tr>
<td>SES</td>
<td>1</td>
<td>187</td>
<td>12.86</td>
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</tr>
<tr>
<td>Gender</td>
<td>1</td>
<td>187</td>
<td>10.47</td>
<td>0.0014</td>
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<td>time*Gender</td>
<td>1</td>
<td>187</td>
<td>8.73</td>
<td>0.0035</td>
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<td>ch*Gender</td>
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<td>187</td>
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<td>rad*Gender</td>
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<td>0.0298</td>
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<td>time</td>
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<td>2.66</td>
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<td>time_rad</td>
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</table>

Fixed effects

| Effect     | ch  | rad | Gender | Estimate | Standard Error | DF  | t Value | Pr > |t| |
|------------|-----|-----|--------|----------|----------------|-----|---------|------|---|
| Intercept  | 98.7117 | 6.5155 |        | 86       | 15.15          | <.0001 |
| SES        | -4.8269 | 1.3462 |        | 187      | -3.59          | 0.0004 |
| Gender     | F    |      |        | 6.2571   | 6.0445         | 187 | 1.53    | 0.1273 |
| time*Gender| F   | M   |        | 2.7503   | 1.0447         | 187 | 2.63    | 0.0092 |
| time*Gender| M   | F   |        | 4.0336   | 1.0991         | 187 | 3.67    | 0.0003 |
| ch*Gender  | W   | F   |        | 12.4467  | 5.1174         | 187 | 2.43    | 0.0159 |
| ch*Gender  | W   | M   |        | -15.7442 | 4.8515         | 187 | -3.25   | 0.0014 |
| ch*Gender  | w/o | F   |        | 0        | 187           |      |         |      |
| ch*Gender  | w/o | M   |        | 0        | 187           |      |         |      |
| rad*Gender | W   | F   |        | -1.9936  | 5.9981         | 187 | -0.33   | 0.7400 |
| rad*Gender | W   | M   |        | 13.6874  | 5.8810         | 187 | 2.33    | 0.0210 |
| rad*Gender | w/o | F   |        | 0        | 187           |      |         |      |
| rad*Gender | w/o | M   |        | 0        | 187           |      |         |      |
| time        | 0    |     |        | 0        | 187           |      |         |      |
| time_rad    | W   | F   |        | -4.7262  | 1.2837         | 187 | -3.68   | 0.0003 |
| time_rad    | w/o | F   |        | 0        | 187           |      |         |      |
| time_sq     | W   | F   |        | -0.3452  | 0.0946         | 68  | -3.65   | 0.0005 |
| time_sq_rad | W   | F   |        | 0.3467   | 0.1072         | 187 | 3.23    | 0.0015 |
| time_sq_rad | w/o | F   |        | 0        |                 |      |         |      |
| rad         | W   |     |        | 0        | 187           |      |         |      |
| rad         | w/o |     |        | 0        | 187           |      |         |      |
| ch          | W   |     |        | 0        | 187           |      |         |      |
| ch          | w/o |     |        | 0        | 187           |      |         |      |

Female in SES class 4 with radiation
Model with variable transformations

Fixed effects

<p>| Effect          | ch  | rad | Gender | Estimate | Standard Error | DF  | t Value | Pr &gt; |t| |
|-----------------|-----|-----|--------|----------|----------------|-----|---------|------|---|
| Intercept       |     |     |        | 26.8187  | 12.7830        | 84  | 2.10    | 0.0389| |
| sesstr1         |     |     |        | 40.8220  | 10.9631        | 257 | 3.72    | 0.0002| |
| time            |     |     |        | 1.8901   | 0.6046         | 80  | 3.13    | 0.0025| |
| time*Gender     | F   |     |        | -1.4398  | 0.5808         | 257 | -2.48   |      |</p>
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</table>

**Female in SES class 4 with radiation**
Table: Comparison of models

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Model without interactions</th>
<th>Model with interactions</th>
<th>Model with variable transformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 Res Log Likelihood</td>
<td>3565.1</td>
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<td>AIC (the smaller the better)</td>
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<td>3207.1</td>
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<td>BIC (the smaller the better)</td>
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</table>
Individual Growth Models for NPS_total and other variables

Model without interaction

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<tr>
<th>Effect</th>
<th>Num DF</th>
<th>Den DF</th>
<th>F Value</th>
<th>Pr &gt; F</th>
</tr>
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<tbody>
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<td>SES</td>
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</tbody>
</table>

Fixed effects

| Effect       | Estimate       | Error      | DF    | t Value | Pr > |t| |
|--------------|----------------|------------|-------|---------|------|---|
| Intercept    | 119.03         | 4.8096     | 16    | 24.75   | <.0001 |
| SES          | -5.9384        | 1.1635     | 413   | -5.10   | <.0001 |
| agegr        | 7.7851         | 2.9770     | 413   | 2.62    | 0.0092 |
| NPS_total    | -2.1518        | 0.4318     | 413   | -4.98   | <.0001 |

Model with interactions

<table>
<thead>
<tr>
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<th>F Value</th>
<th>Pr &gt; F</th>
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Fixed effects

| Effect       | Gender | Estimate       | Error      | DF    | t Value | Pr > |t| |
|--------------|--------|----------------|------------|-------|---------|------|---|
| Intercept    |        | 119.03         | 4.8096     | 14    | 24.02   | <.0001 |
| SES          |        | -5.9384        | 1.1635     | 413   | -5.10   | <.0001 |
| SES*Gender   | F      | -3.6049        | 1.2299     | 413   | -2.93   | 0.0036 |
| SES*Gender   | M      | -5.5395        | 1.9663     | 413   | -2.82   | 0.0051 |
| agegr        |        | 7.4935         | 2.4384     | 413   | 3.07    | 0.0023 |
| Gender       | F      | 18.0098        | 6.4601     | 413   | 2.79    | 0.0056 |
| Gender       | M      |                |            |       |         |      |   |
| NPS_total    |        | -2.2464        | 0.4275     | 413   | -5.26   | <.0001 |

Model with variable transformations

<table>
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<th>Pr &gt; F</th>
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Fixed effects

| Effect                  | Gender | Estimate | Standard Error | DF  | t Value | Pr > |t| |
|-------------------------|--------|----------|----------------|-----|---------|------|---|
| Intercept               |        | 41.2304  | 12.4293        | 85  | 3.32    | 0.0013|
| sestr1                  |        | 24.5774  | 12.7157        | 340 | 1.93    | 0.0541|
| sestr1*Gender           | F      | 51.9852  | 22.1714        | 340 | 2.34    | 0.0196|
| sestr1*Gender           | M      |          |                |     |         |      |
| Gender                  | F      | -28.6059 | 13.6342        | 340 | -2.10   | 0.0366|
| Gender                  | M      |          |                |     |         |      |
| agedxtr1                |        | 10.9135  | 11.1550        | 340 | 0.98    | 0.3286|
| agedxtr1*totaltr1       |        | -1172.64 | 358.41         | 340 | -3.27   | 0.0012|
| totaltr1                |        | 118.71   | 226.30         | 340 | 0.52    | 0.6002|
| totaltr2                |        | 235.17   | 79.3502        | 340 | 2.96    | 0.0033|

Table: Comparison of models

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Model without interactions</th>
<th>Model with interactions</th>
<th>Model with variable transformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 Res Log Likelihood</td>
<td>3677.6</td>
<td>3664.0</td>
<td>3254.6</td>
</tr>
<tr>
<td>AIC (the smaller the better)</td>
<td>3681.6</td>
<td>3668.0</td>
<td>3258.6</td>
</tr>
<tr>
<td>AICC (the smaller the better)</td>
<td>3681.6</td>
<td>3668.1</td>
<td>3258.6</td>
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<tr>
<td>BIC (the smaller the better)</td>
<td>3683.4</td>
<td>3669.9</td>
<td>3263.7</td>
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</table>

id=5