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LONGITUDINAL CURVES FOR BEHAVIORS OF CHILDREN DIAGNOSED WITH A BRAIN TUMOR

by

Huayan Chai

Under the Direction of Yu-Sheng Hsu

ABSTRACT

Change in adaptive outcomes of children who are treated for brain tumors is examined using longitudinal data. The children received different types of treatment from none to any combinations of three treatments, which are surgery, radiation and chemotherapy. In this thesis, we use mixed model to find the significant variables that predict change in outcomes of communication skill, daily living skills and socialization skill. Fractional polynomial transformation method and Gompertz method are applied to build non-linear longitudinal curves. We use PRESS as the criterion to compare these two methods. Comparison analysis shows the effect of each significant variable on adaptive behaviors over time. In most cases, model with Gompertz method is better than that with Transformation method. Significant predictors of change in adaptive outcomes include Time, Gender, Surgery, SES classes, interaction between Time and Radiation, interaction between Time and Gender, interaction between Age and Gender.

INDEX WORDS: Mixed Model, Fractional Polynomial Transformation, Gompertz Model, Press

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by

Huayan Chai

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Master of Science

in the College of Arts and Sciences

Georgia State University

2007

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Jiawei Liu

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List of Abbreviations

SES	Socioeconomic Status
VABS	Vineland Adaptive Behavior Scales
COMMSS	Communication Standard Scores
DLSS	Daily Living Standard Scores
SOCSS	Socialization Standard Scores

Chapter One: Introduction

With support provided by Brain & Behavior Research Fellowship at Georgia State University, the adaptive behaviors of children who have received treatments for brain tumors are analyzed in this thesis.

CBTRUS reported that the incidence rate of childhood primary non-malignant and malignant brain and central nervous system tumors is 4.3 cases per 100,000 person-years [6]. The report shows that the number of child brain tumor survivors has significantly increased in recent years with the advances in medical treatments. The treatment for brain tumors usually contains combinations of these: surgery, radiation therapy, and chemotherapy, such as surgery alone, surgery plus chemo.

In some cases the definitive treatment is surgery. In most, however, surgery serves as a temporizing measure that will keep a child out of trouble for long enough to get through definitive therapy that will hopefully eliminate of the tumor. Brain surgery is usually the easiest part of a child's treatment. See [14].

Because the developing brain of a child is so very sensitive to radiation therapy, it is deliberately limited. The irony of effective radiation therapy is that when it works well, the brain damage it causes might exceed that done by the original tumor. See [14].

Chemotherapy only required for the more aggressive tumors. As a rule, chemotherapy should be even more aggressive than the tumor itself. See [14].

There are some other descriptions about these three treatments. For more information, please see reference [12] and [13].

The Vineland Adaptive Behavior Scales(VABS) is a commonly used measure of adaptive functions, that examines personal and social skills used for everyday living. This assessment provides critical data for the diagnosis or evaluation of a wide range of disabilities, including mental retardation, developmental delays, functional skills impairment, and speech/language impairment. VABS has also been proven to be an accurate resource for predicting autism and Asperger syndrome, among other differential diagnoses. The VABS covers a wide range of adaptive behaviors: communication, daily living skills, socialization and motor skills. The more details of VABS can be found in [1].

Although the survival rate of patients with brain cancer has been increased in recent years, the survivors are continuous exposing to the high risk of altered cognitive and behavioral functioning. Researchers at Georgia State University (Tricia King, Robin Morris and Yu-Sheng Hsu) and Emory University (Nicolas Krawiecki) are examining change in childhood adaptive outcomes over time following diagnosis of brain tumor and identifying the demographic and treatment variables that will be most predictive of adaptive outcomes trajectories. The children in this research received none or any combinations of these three treatments. VABS raw scores of communication skill, daily living skills and socialization skill were provided by parents of these patients. The standard scores were obtained by adjusting raw scores relative to the children their same age. Data in this thesis is from 119 children treated for brain tumors, including 529 observations. On average, there are about 4.45 observations per child. The range of observation per child is 2 to 10 and the standard deviation is 2.3. The potentially predictive variables included in this thesis are gender, age at diagnosis,

Socioeconomic Status (SES), surgery, chemotherapy and radiation, and time since diagnosis.

This thesis is organized in the following order. Chapter 1 is the introduction. In Chapter 2, theory of mixed model is introduced and significant variables for communication, daily living skills and socialization are found by mixed models. In Chapter 3, fractional polynomial transformation method and Gompertz method are introduced. Graphics of longitudinal curves from these two methods are provided. Method of PRESS is presented. In Chapter 4, analysis of those curves is presented. Graphics on comparison are provided. In Chapter 5, conclusion from the studies and future research are presented.

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

Variables	Patients					Observations				
	with		without			with		without		
Surgery	93		26			433		96		
Chemo	33		86			151		378		
Radiation	90		29			310		219		
	Patients					Observations				
boys	62					291				
girls	57					238				
age<=8 years old	79					391				
age>8 years old	40					138				
	Patients					Observations				
	1	2	3	4	5	1	2	3	4	5
SES classes	13	28	32	33	12	56	164	150	138	51

Table 1.2. Descriptive Table of COMMSS, DLSS, SOCSS and Time

Variables	Mean	Standard Deviation	Range
COMMSS	86.51704545	17.65545465	34 to 129
DLSS	90.07765152	17.46038163	20 to 134
SOCSS	91.73003802	16.26270436	24 to 131
Time(months between diagnosis and measurement)	43.28670447	37.80728425	0.16667 to 194.7

Chapter Two: Analysis of Significances

In this chapter, the method for finding the significant variables and the results are presented. The repeated measurements were taken on each child occurred over time. Parents of these children completed the VABS annually, typically beginning at the time of diagnosis. Mixed models were used for analyzing significance of variables. To explain the change over time of standard scores of Communication Skill, Daily Living Skills and Socialization Skill, the variables which we are interested in are Months between date of diagnosis and date of exam (Time), Gender, age at diagnosis, SES classes, Treatments (surgery, radiation and chemotherapy), and interactions of these variables. The patients are assumed to be random and other variables are fixed effects in the model. Gender, SES classes, Surgery, Chemotherapy and Radiation are categorical variables. Time and Age are treated as continuous variables in this chapter.

2.1 The Mixed Model

The mixed model extends the general linear model by allowing a more flexible specification of the covariance matrix of error. It allows for both correlation and heterogeneous variances.

The mixed model can be written as

$$\mathbf{y} = \mathbf{X}\beta + \mathbf{Z}\gamma + \varepsilon$$

Where **y** denotes the vector of observed values, **X** is the known matrix of explanatory variables, β is the unknown fixed-effect parameter vector, **Z** is the known design

matrix of random effects, γ is the unknown random parameter and ε is the unobserved vector of independent and identically distributed Gaussian random errors. In this thesis, the correlation matrix **R** is assumed to have the structure of compound symmetry.

$$\mathbf{R} = \begin{pmatrix} 1 & \rho & \dots & \rho \\ \rho & 1 & \dots & \rho \\ \dots & \dots & \dots & \dots \\ \rho & \rho & \dots & 1 \end{pmatrix}$$

2.2 Significant variables

SAS PROC MIXED was used to fit mixed models using VABS standardized scores as response variables, including scaled scores of Communication, Socialization and Daily Living Skills. All the significant variables were chosen with p-value less than 0.05.

The table 2.1 shows the results of significant predictive variables using standard scores. For Communication Skill, significant variables are Gender, Surgery, SES Class, Time*Surgery and Age*Gender, where * represents their interaction. For Daily Living Skills, there are three significant variables, Time, Time*Surgery and Time*Gender. For Socialization Skill, significant variables are Gender, Surgery, SES Classes and Age*Gender. Since in this study the focus is on the behavioral change over time, Socialization skill has no significant relationship with time so it is not included in the remainder of the analyses.

Table 2.1 Predictive variables and their p-values

STANDARD SCORES			
Effect	Communication p-value	DailyLiving p-value	Socialization p-value
Time	0.1742	**0.0153**	0.7533
Age	0.4582	0.2546	0.6669
Gender	**0.013**	0.0848	**0.0478**
Surgery	**0.0252**	0.0749	**0.0194**
Chemo	0.9509	0.8059	0.5636
Radiation	0.594	0.8127	0.8244
SES Classes	**0.0104**	0.1906	**0.0263**
Time*Age	0.9251	0.1248	0.1223
Time*Surgery	0.4929	0.1664	0.8088
Time*Chemo	0.1778	0.2677	0.6468
Time*Radiation	**0.0246**	**0.0011**	0.0982
Time*Gender	0.5393	**0.0179**	0.2663
Time*SES Classes	0.5218	0.2759	0.904
Age*Gender	**0.008**	0.3622	**0.0146**
Gender*Surgery	0.5061	0.8422	0.9684
Gender*Chemo	0.562	0.7899	0.8512
Gender*Radiation	0.1097	0.3842	0.2234
Gender*SES Classes	0.065	0.3604	0.236

Chapter Three: Longitudinal Curves

In this chapter, longitudinal curves for VABS scaled scores are presented and discussed. Two methods are applied to find the proper curves. One is fractional polynomial transformation with mixed regression model ('Transformation' will represent this method in this thesis). Another method is Gompertz non-linear mixed model ('Gompertz' will represent this method in this thesis), which is a common used method for growth curve. We will use PRESS as the criterion to compare these two methods.

3.1 Fractional Polynomial Transformation

In this thesis, fractional polynomial transformation was used with one continuous variable model. For simplicity, the transformation procedure is described with single continuous variable model, which is

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

Where $\boldsymbol{\beta}$ denotes the vector of model parameters. This function is generalized as

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

The functions $F_j(x)$ are a particular type of power function.

$$F_1(x) = x^{p_1}$$

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

where p_j 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. In this thesis, we chose J = 1 and J = 2. For J = 1, 8 models from $p_1 \in \mathrm{P}$ are fitted. The best model is the one with the largest log likelihood. For J = 2, 36 models form the distinct pairs of powers, $(p_1, p_2) \in \mathrm{P} \times \mathrm{P}$, are fitted. Again the best model is the one with the largest log likelihood.

The partial likelihood ratio test is used to test whether either of the two best models is significantly better than the linear model. 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 is approximately distributed as χ^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 is approximately distributed as χ^2 with 2 degree of freedom under the null hypothesis that the second function is equal to zero. For further details of this transformation, see [2].

In this thesis, SAS MACRO coding and SAS PROC MIXED is applied to Transformation method.

3.2 Gompertz Non-linear Mixed Model

Gompertz curve [3] is a commonly used function to model a growth curve. The function can be defined as:

$$y(x) = A_0 \exp\left(\exp(b_0) \frac{\exp(b_1 x) - 1}{b_1} \right)$$

It is based on a simple foundation: for this Gompertz curve, the logarithm of the relative growth rate $r(x)$ at x, defined as the ratio of the growth velocity dy/dx to the attained growth $y(x)$:

$$r(x) = \frac{1}{y}\frac{dy}{dx} = \frac{d \ln y}{dx}$$

is a linear function of x:

$$\ln r(x) = b_0 + b_1 x$$

In this thesis, SAS PROC NLMIXED is applied to Gompertz model.

3.3 PRESS residuals

The residual is defined to be the difference between the predicted value evaluated through the estimated model, and the observed value. Since the estimated model is derived from all observations including the one we want to predict, the residual tends to be smaller than it is supposed to be. This is what we defined as the "shrinkage". One way to find more reasonable residual is to take away the observation we want to predict in the process of estimating the model. In the other words, using n-1 (n is the sample size) observations to estimate the model leaving one observation out. The PRESS residual is the difference between the estimated value on this observation

and the true observed value. PRESS statistic is defined to be the sum of square PRESS residuals, which includes all n observations. It can be expressed as

$$\sum_{i=1}^{n}(\hat{Y}_{(-i)} - Y_i)^2,$$

where Y_i is the *i*th observation and $\hat{Y}_{(-i)}$ is the estimated Y_i without using the *i*th observation, i = 1, 2, …, n.

In this thesis, PRESS values were calculated from both Transformation method and Gompertz method. PRESS for Transformation method can be obtained from SAS PROC MIXED. The SAS MACRO coding is used for Gompertz models in this thesis to calculate the PRESS since there is no PRESS output of SAS PROC NLMIXED. The program can be seen in Appendix C.

3.4 Longitudinal Curves

We have found the significant predictive variables for communication and daily living skills in chapter 2. In this chapter, data is divided into different groups, such as boys who are in SES class 3 with treatments of surgery and radiation. Some groups which have few patients and observations were not included since the models may not be reliable. The variable Age is treated to be categorical in this chapter and grouped into younger children, who are younger than or equal to 8 years old, and older children, who are older than 8 years old.

For each group, two curves are created from Transformation method and Gompertz method. The better model from these two methods is the one which have smaller PRESS value. Table 3.1 and 3.2 show the PRESS values of Transformation

method and Gompertz method for each model. In the most models, Gompertz method is better than Transformation method.

Table 3.1. PRESS for models of communication scaled scores.

Models of Communication Scaled Scores					
sex	surgery	radiation	sesclass	Transformation PRESS	Gompertz PRESS
male	yes	yes	3	6386.786	7235.448
male	yes	yes	4	8287.089	5617.978
male	yes	no	2	5185.081	3755.141
male	yes	no	3	11956.93	11567.94
female	yes	yes	2	353191.9	10130.41
female	yes	yes	3	12663.84	9081.575
female	yes	yes	4	16001.2	9696.771
female	yes	no	2	7146.251	8225.01
female	yes	no	4	10459.23	7806.219

Table 3.2. PRESS for models of daily living skills scaled scores.

Models of Daily Living Skills Scaled Scores			
sex	radiation	Transformation PRESS	Gompertz PRESS
male	yes	50082.92	49687.77
male	no	25587.92	25839.19
female	yes	44197.49	43153.58
female	no	69212.97	36653.45

From figure 3.1 to figure 3.13, there are two curves in each figure, one with Fractional Polynomial Transformation method, another with Gompertz method. In most cases these two curves are pretty similar. Under each graph, the model from Transformation method and Gompertz method are presented.

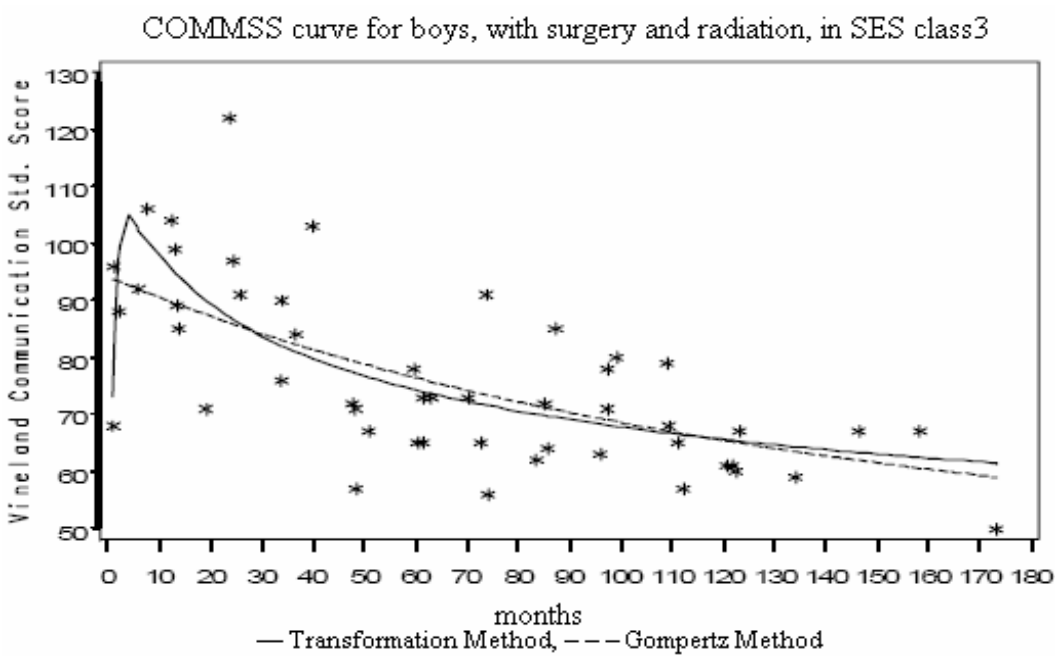

Figure3.1. COMMSS for boys, surgery, radiation, SES class3.

In this group, there are 8 patients and total 51 observations.

Transformation method: $\hat{y} = 28.2386 + 44.9219 * x^{-0.5} + 76.1274 * x^{-0.5} * \ln x$.

Gompertz method: $\hat{y} = 94.0589 * \exp\left[- \exp(-5.251) \frac{\exp((-0.00491) * x) - 1}{-0.00491} \right]$.

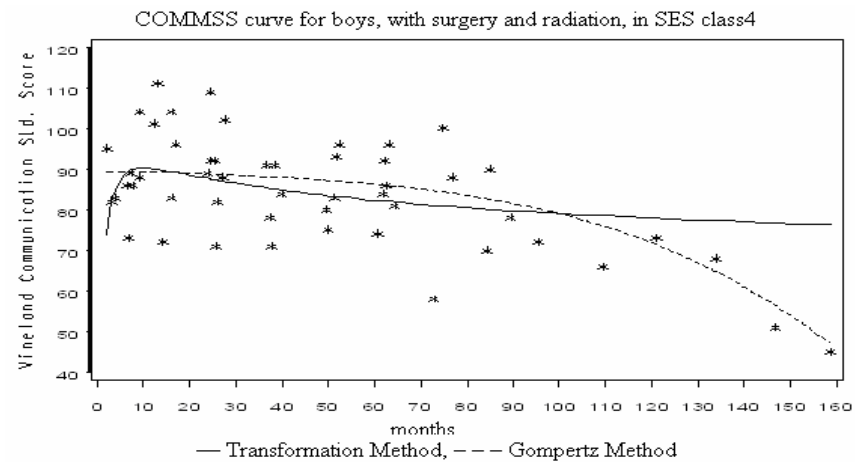

Figure3.2. COMMSS for boys, surgery, radiation, SES class4.

In this group, there are 11 patients and total 51 observations.

Transformation method: $\hat{y} = 55.7978 - 15.2352 * x^{-0.5} + 53.8751 * x^{-0.5} * \ln(x)$.

Gompertz method: $\hat{y} = 89.5164 * \exp\left[- \exp(-8.3083) \frac{\exp((0.02681) * x) - 1}{0.02681} \right]$.

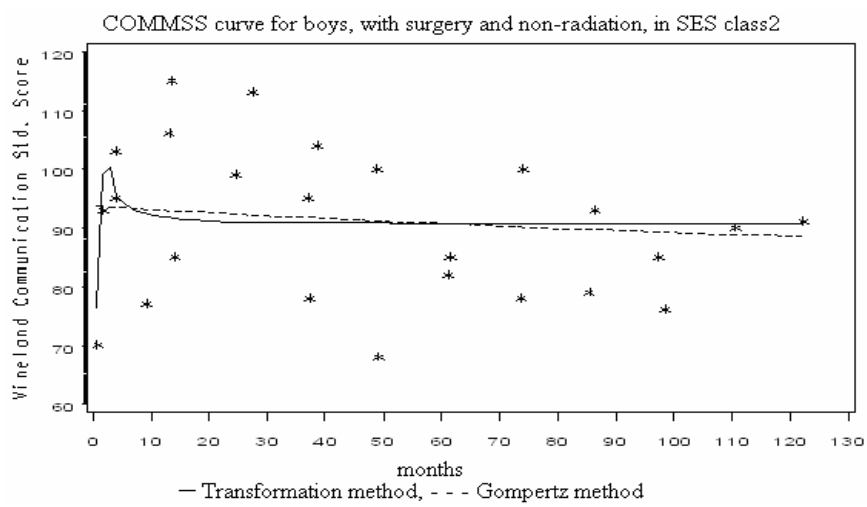

Figure3.3. COMMSS for boys, surgery, non-radiation, SES class2.

In this group, there are 4 patients and total 25 observations.

Transformation method: $\hat{y} = 90.5238 - 70.2713 * x^{-2} + 73.1317 * x^{-1.5}$.

Gompertz method: $\hat{y} = 93.6573 * \exp\left[- \exp(-7.3879) \frac{\exp((-0.00490) * x) - 1}{-0.00490} \right]$.

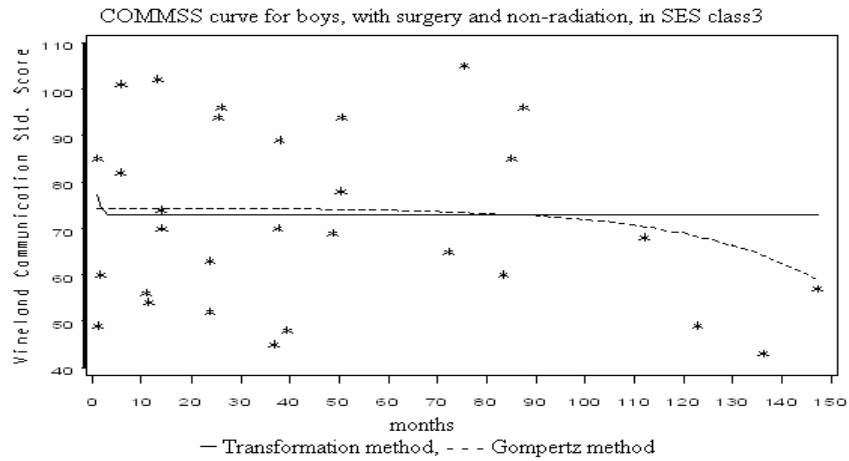

Figure3.4. COMMSS for boys, surgery, non-radiation, SES class3.

In this group, there are 8 patients and total 30 observations.

Transformation method: $\hat{y} = 72.7302 + 3.4986 * x^{-2} + 2.1862 * x^{-1.5}$.

Gompertz method: $\hat{y} = 74.2714 * \exp\left[- \exp(-10.7334) \frac{\exp((0.04133) * x) - 1}{0.04133} \right]$.

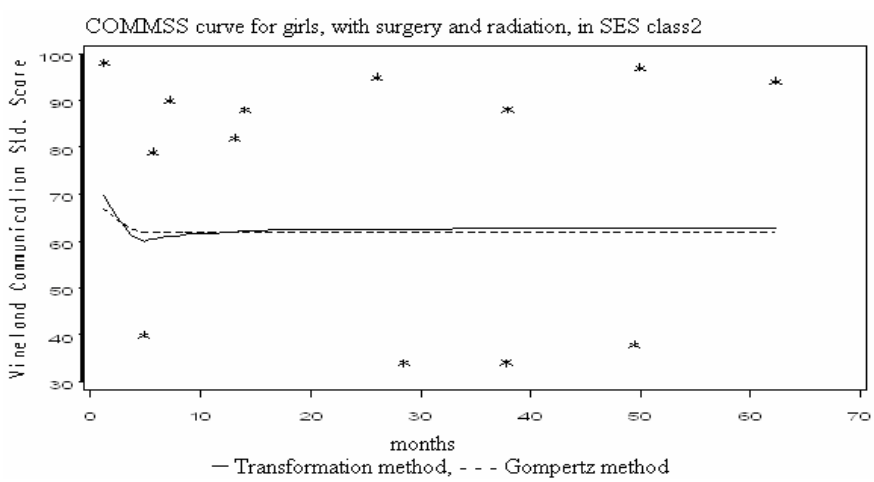

Figure3.5. COMMSS for girls, surgery, radiation, SES class2.

In this group, there are 4 patients and total 13 observations.

Transformation method: $\hat{y} = 63.0077 - 70.2719 * x^{-1.5} + 86.4758 * x^{-2}$.

Gompertz method: $\hat{y} = 123.58 * \exp\left[- \exp(0.2407) \frac{\exp((-1.8429) * x) - 1}{-1.8429} \right]$.

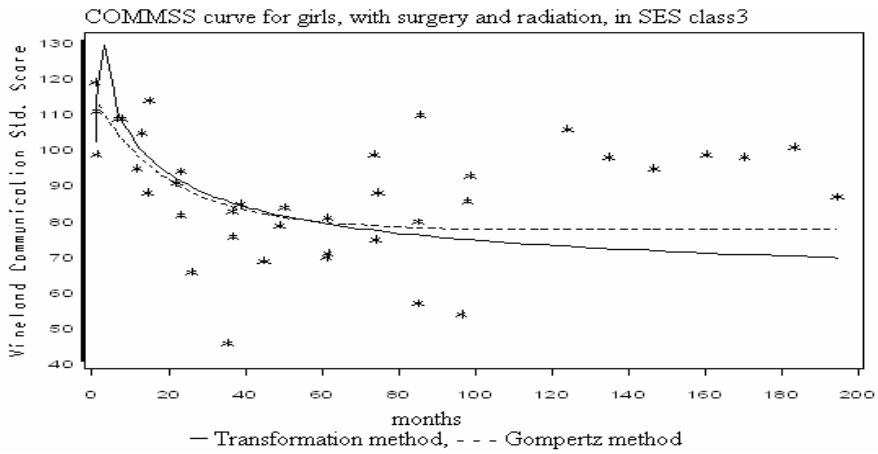

Figure3.6. COMMSS for girls, surgery, radiation, SES class3.

In this group, there are 8 patients and total 39 observations.

Transformation method: $\hat{y} = 55.4506 + 199.23 * x^{-0.5} - 149.58 * x^{-1}$.

Gompertz method: $\hat{y} = 115.3 * \exp\left[- \exp(-4.0193) \frac{\exp((-0.04404) * x) - 1}{-0.04404} \right]$.

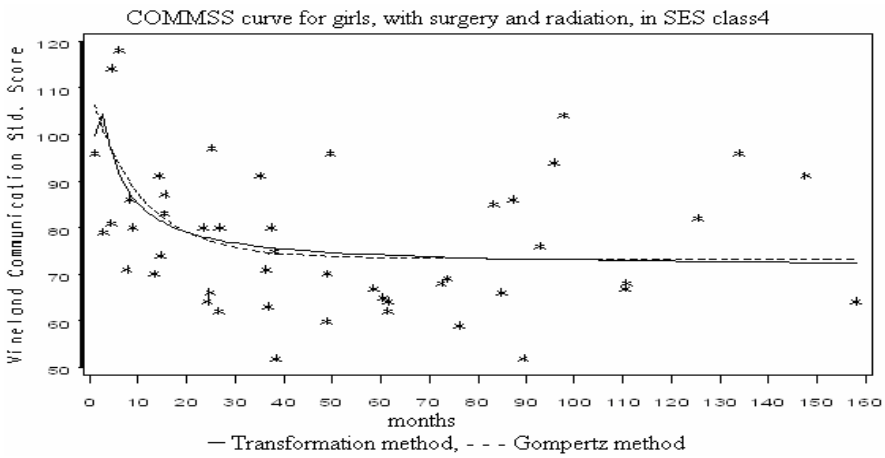

Figure3.7. COMMSS for girls, surgery, radiation, SES class4.

In this group, there are 11 patients and total 48 observations.

Transformation method: $\hat{y} = 71.3198 - 165.07 * x^{-1.5} + 190.10 * x^{-1}$.

Gompertz method: $\hat{y} = 110.01 * \exp\left[- \exp(-3.3654) \frac{\exp((-0.08537) * x) - 1}{-0.08537} \right]$.

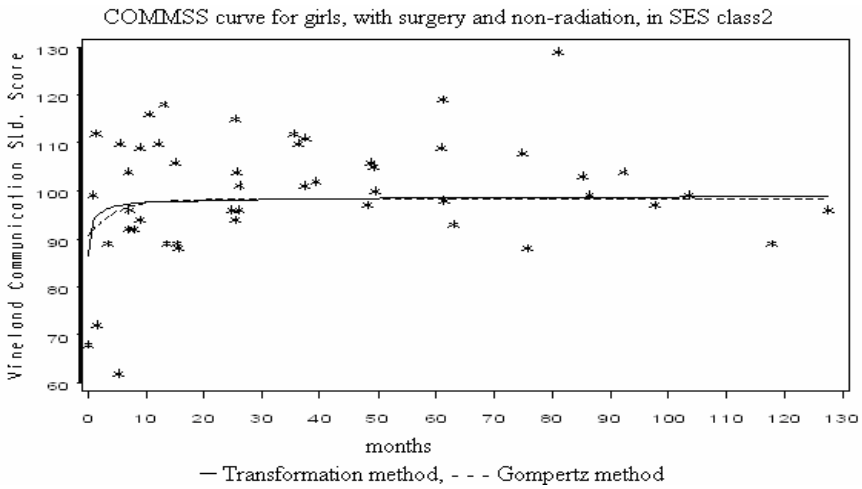

Figure 3.8. COMMSS for girls, surgery, non-radiation, SES class2.

In this group, there are 9 patients and total 49 observations.

Transformation method: $\hat{y} = 99.2026 - 5.1843 * x^{-0.5}$.

Gompertz method: $\hat{y} = 90.3073 * \exp\left[\exp(-3.9088)\dfrac{\exp((-0.2363) * x) - 1}{-0.2363}\right]$.

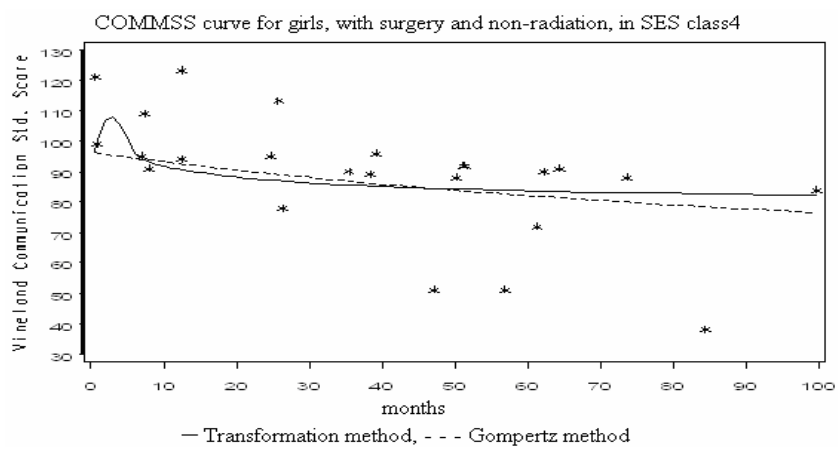

Figure 3.9. COMMSS for girls, surgery, non-radiation, SES class4.

In this group, there are 5 patients and total 24 observations.

Transformation method: $\hat{y} = 76.4980 + 60.2018 * x^{-0.5} - 36.5616 * x^{-1}$.

Gompertz method: $\hat{y} = 96.286 * \exp\left[-\exp(-5.6904)\dfrac{\exp((-0.00828) * x) - 1}{(-0.00828)}\right]$.

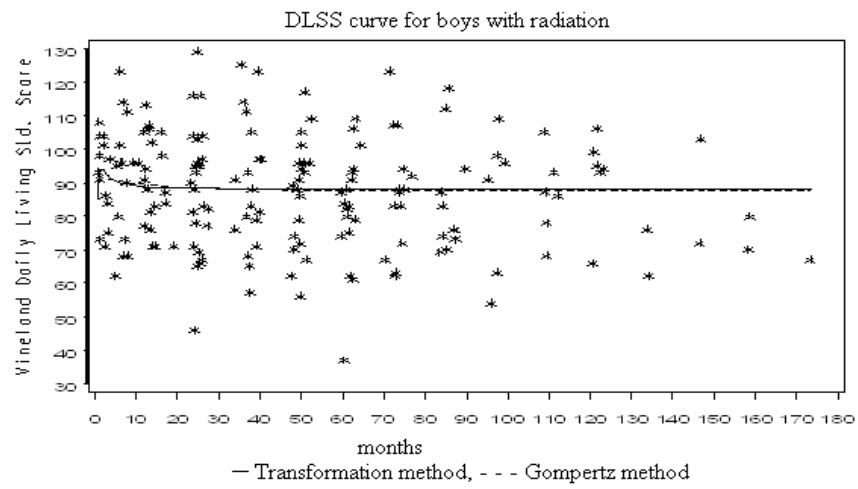

Figure 3.10. DLSS for boys, radiation.

In this group, there are 36 patients and total 180 observations.

Transformation method: $\hat{y} = 87.8445 + 52.8074 * x^{-1.5} - 50.1841 * x^{-2}$.

Gompertz method: $\hat{y} = 92.1755 * \exp\left[- \exp(-5.5353) \frac{\exp((-0.07881) * x) - 1}{(-0.07881)} \right]$.

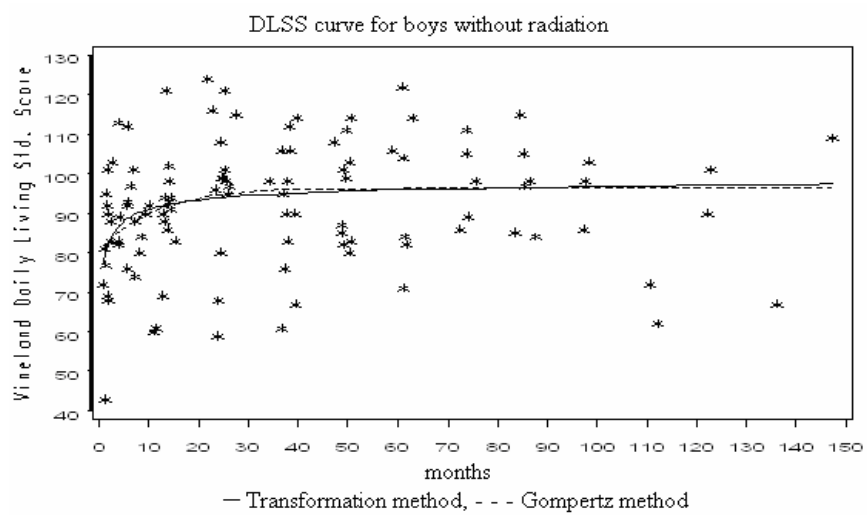

Figure 3.11. DLSS for boys, non-radiation.

In this group, there are 26 patients and total 110 observations.

Transformation method: $\hat{y} = 99.7346 - 30.3621 * x^{-0.5} + 9.5250 * x^{-1}$.

Gompertz method: $\hat{y} = 80.7598 * \exp\left[\exp(-4.1085) \frac{\exp((-0.09243) * x) - 1}{(-0.09243)} \right]$.

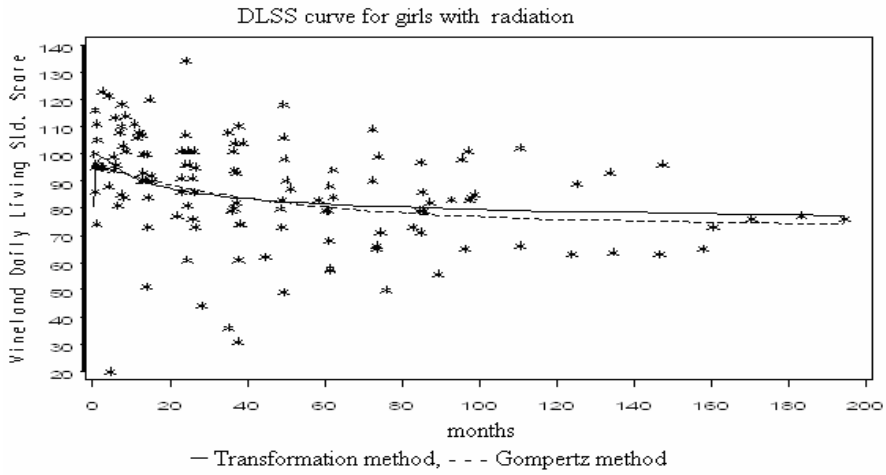

Figure 3.12. DLSS for girls, radiation.

In this group, there are 33 patients and total 129 observations.

Transformation method: $\hat{y} = 71.8219 + 83.6263 * x^{-0.5} - 64.9451 * x^{-1}$.

Gompertz method: $\hat{y} = 96.4896 * \exp\left[- \exp(-5.2802) \frac{\exp((-0.01908) * x) - 1}{(-0.01908)} \right]$.

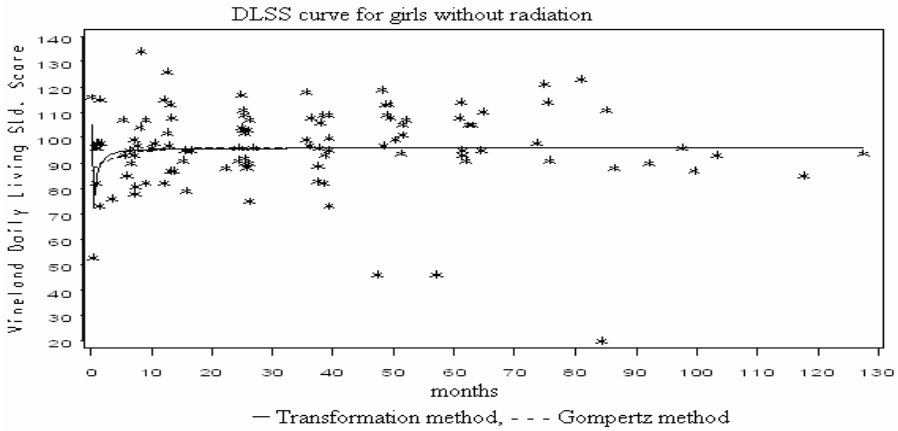

Figure 3.13. DLSS for girls, non-radiation.

In this group, there are 23 patients and total 109 observations.

Transformation method: $\hat{y} = 95.894 - 17.449 * x^{-1.5} + 7.3827 * x^{-2}$.

Gompertz method: $\hat{y} = 87.1258 * \exp\left[\exp(-3.827) \frac{\exp((-0.2241) * x) - 1}{(-0.2241)} \right]$.

Chapter four: Comparison Analysis

In this chapter, the focus is on the effects of each variable on adaptive behaviors over time. There are four variables having significant relationships to communication skill over time - Gender, SES class, Radiation and Surgery. Gender and Radiation have a significant relationship to daily living skills over time. Chemotherapy is not a significant variable. So in all comparisons in this chapter, patients may or may not have the treatment of chemotherapy.

Since there is not enough data available for the situation of non-surgery, the comparison between surgery and non-surgery can not be conducted. The comparison between boys and girls, between radiation and non- radiation and among SES classes are studied for each available group. All the graphics for comparison are drawn by using SAS PROC GPLOT.

4.1 Comparison among SES Classes

There are five levels for SES classes. Class 1 is the highest level and class 5 is the lowest level. There are four groups available for analysis and all of them are on communication skill.

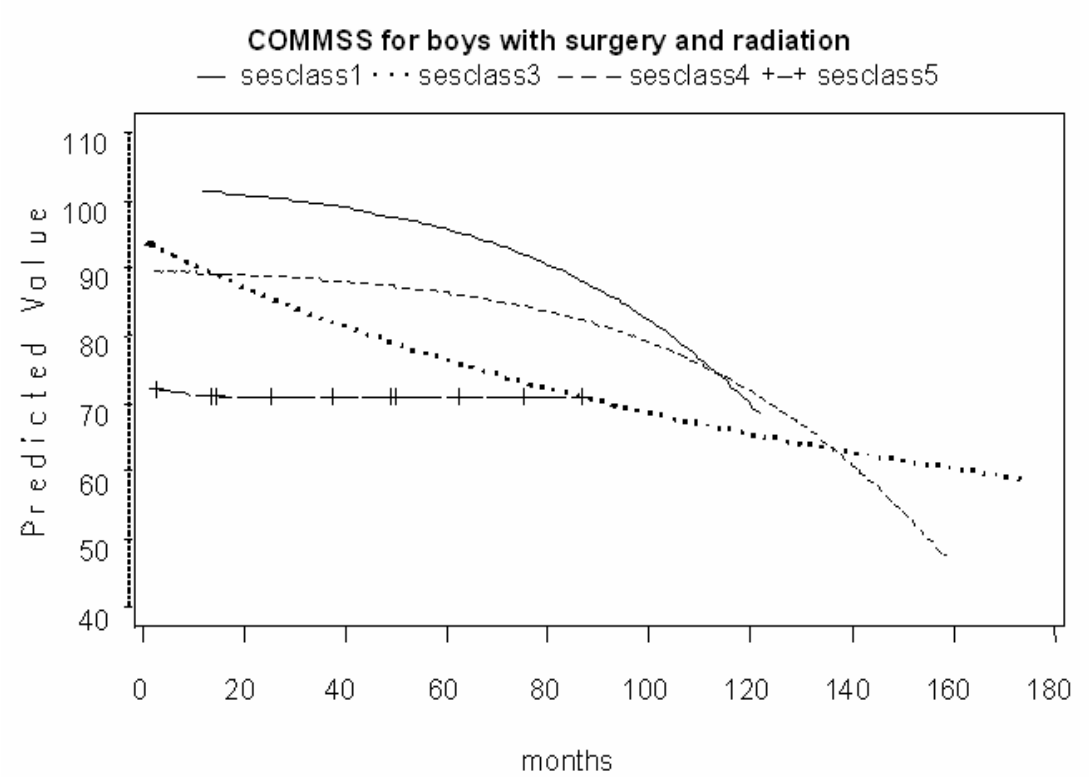

Figure 4.1. Curves of communication standard score for boys with treatments of surgery and radiation.

Figure 4.1 shows curves of communication skill for the boys with treatments of surgery and radiation. In this group, there are 3 patients and 16 observations for SES class 1, 8 patients and 51 observations for SES class 3, 11 patients and 51 observations for SES class 4 and 2 patients and 11 observations for SES class 5. Since there is few data available for SES class 1 and 5, these two curves are ignored. Curve of class 4 falls more slowly than that of class 3 before seven years while it falls more quickly than that of class 3 after seven years. In this group, boys in SES class 4 seem to outperform SES class 3 for the first 10 years, and behave otherwise after 10 years.

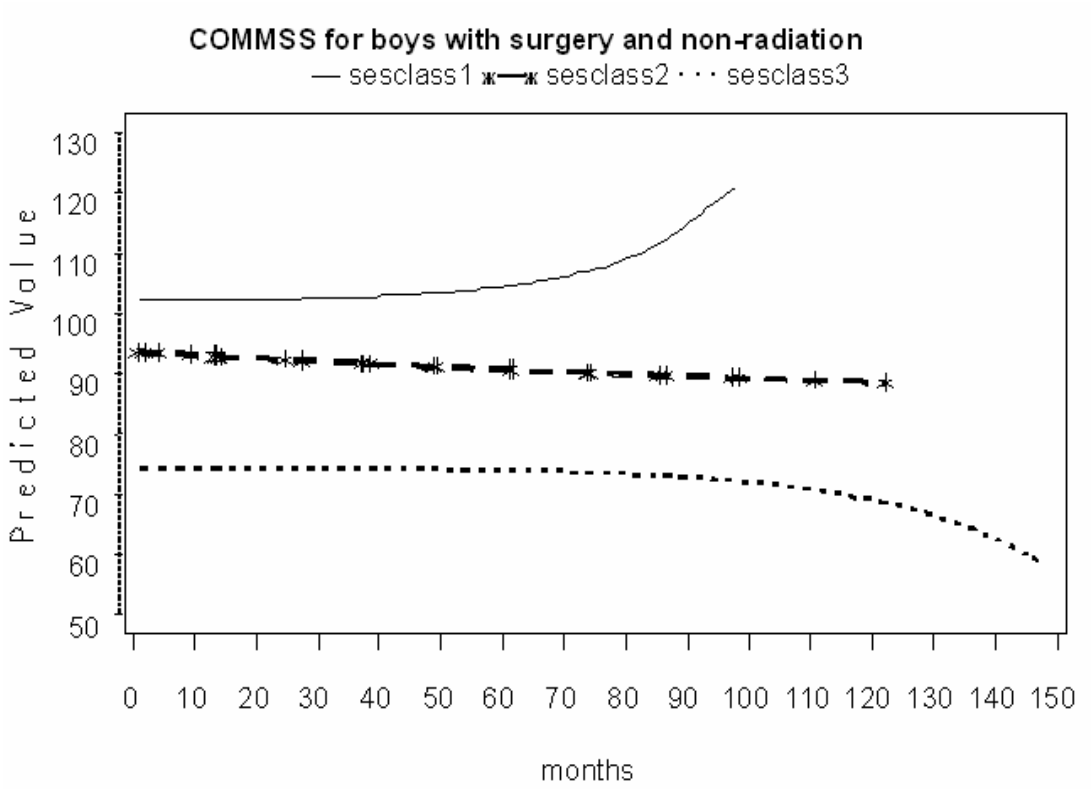

Figure 4.2. Curves of communication standard scores for boys with treatments of surgery and non-radiation.

Figure 4.2 shows curves of communication skill for boys with surgery and no radiation. In this group, there are 2 patients and 14 observations for SES class 1, 4 patients and 25 observations for SES class 2 and 8 patients and 30 observations for SES class 3. Curve of SES class 2 and class 3 keep flat for almost 10 years. Since there is few data available for SES class 1, curve of class 1may not be reliable. In this group, it can be seen that the patients in the higher SES class have a little bit better trend of communication skill than those in lower SES classes.

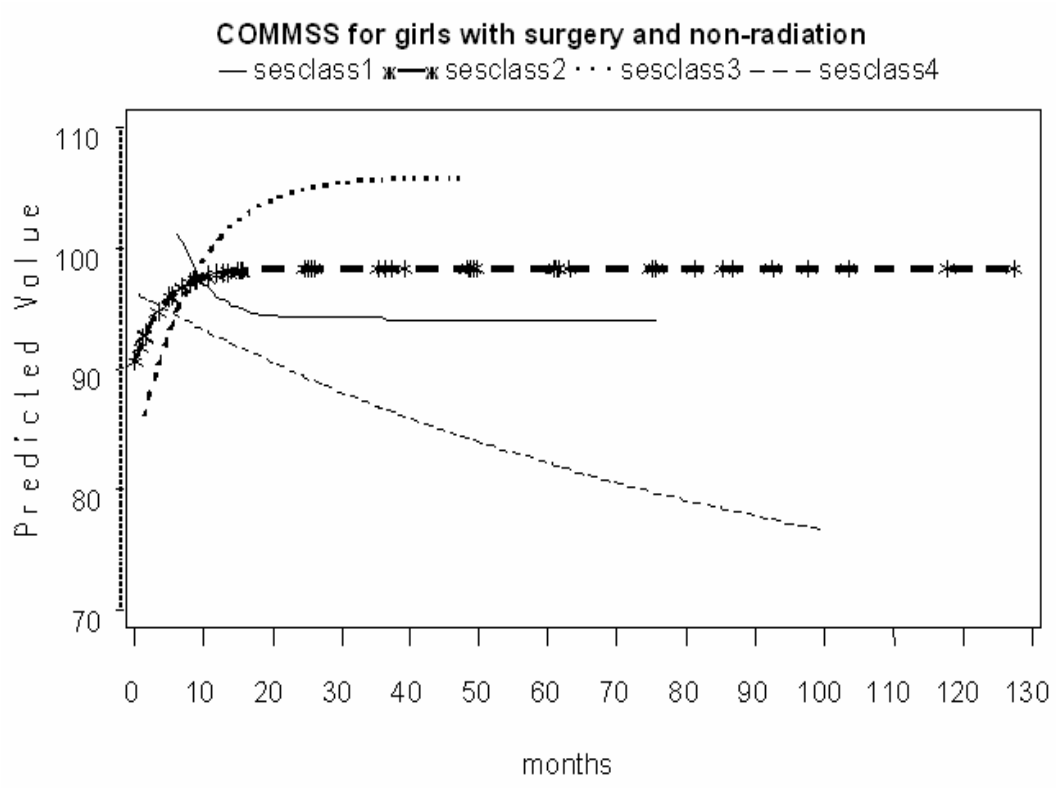

Figure 4.3. Curves of communication standard score for girls with treatments of surgery and non-radiation.

Figure 4.3 shows curves of communication skill for girls with surgery and no radiation. In this group, there are 3 patients and 12 observations for SES class 1, 9 patients and 49 observations for SES class 2, 3 patients and 13 observations for SES class 3 and 5 patients and 24 observations for SES class 4. We will not make any comments on SES classes 1 and 3 due to their small sample sizes. Curve of SES class 2 goes up for the first year and half and then keeps flat afterward. Curve of class 4 goes down almost at the same rate. In this group, it is clear that the higher SES class patients yield the better result on the trend of communication skill over time.

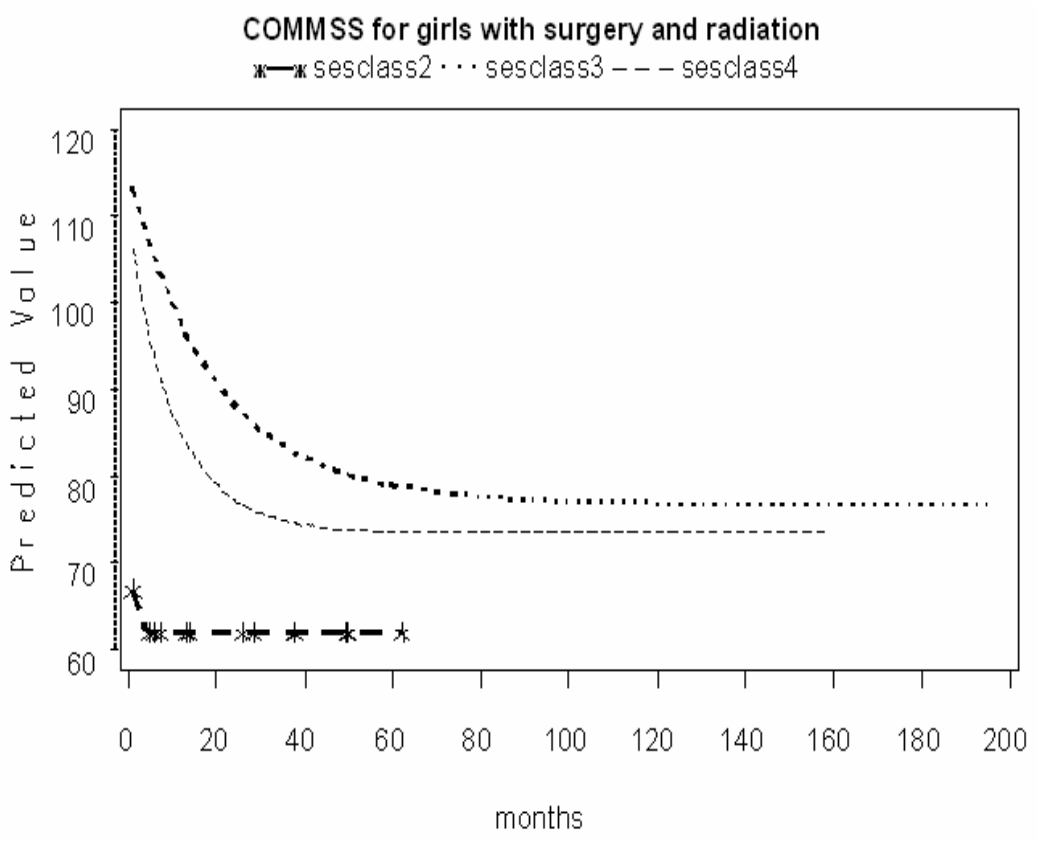

Figure 4.4. Curves of communication standard scores for girls with treatments of surgery and radiation.

As shown in figure 4.4, for girls with treatments of surgery and radiation, there are 4 patients and 13 observations for SES class 2, 8 patients and 39 observations for SES class 3 and 11 patients and 18 observations for SES class 4. Both curves of SES classes 3 and 4 go down for the first three years, and then keep flat. Curve of SES class 2 keeps low and flat all time. It might due to the small sample size again. Since the curve of SES class 3 is always above that of SES class4, it seems that the girls in the higher SES classes performed better on communication skill over time for this group.

4.2 Comparison between boys and girls

There are five groups available for this comparison, three of them regarding to communication skill and two of them daily living skills. Comparison between boys and girls is to discover the difference performance of them.

In figure 4.5, curves of communication standard scores are shown for children in SES class 2 with surgery and non-radiation. In this group, there are 4 patients and 25 observations for boys and 9 patients and 49 observations for girls. Curve of boys keeps falling down almost in a constant rate. The curve of girls goes up quickly in first one year and then becomes flat. In this group, girls look like having a better performance than boys.

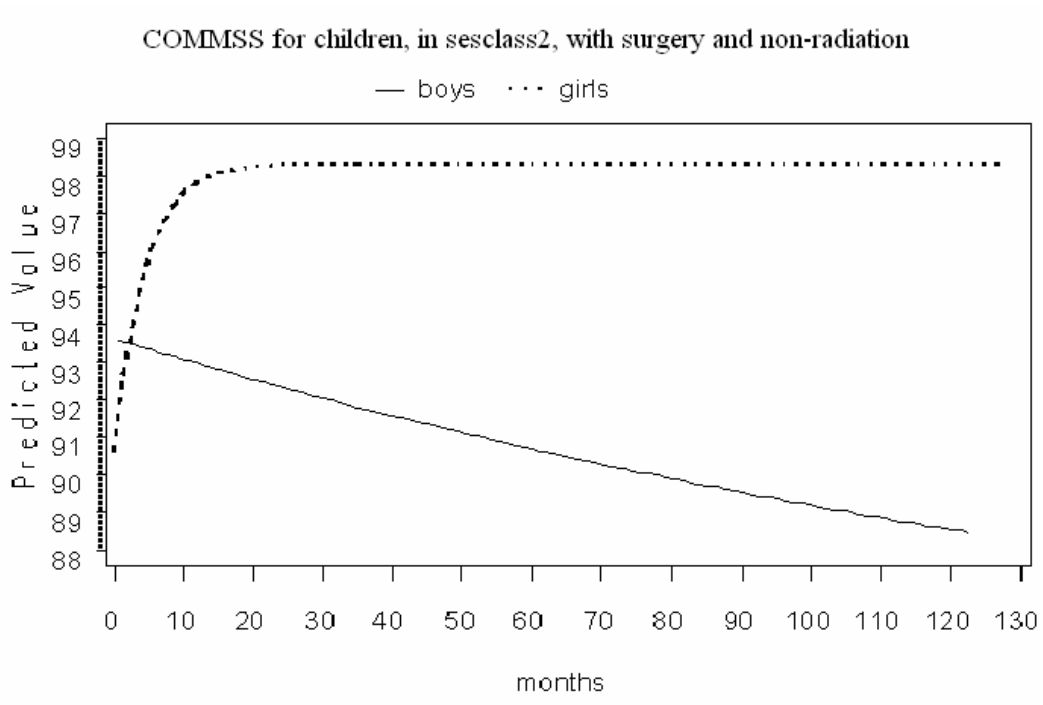

Figure 4.5. Curves of communication standard scores for children who are in SES class 2 and with treatments of surgery and non-radiation.

In figure 4.6, communication skills are compared between boys and girls who are in SES class 3 and with treatments of surgery and radiation. In this group, there are 8 patients and 51 observations for boys and 8 patients and 39 observations for girls. Both curves for boys and girls are concave upward. They may not have much difference in shape. However, the girl's curve seems to be always above the boy's curve. Therefore, the girls have a better trend of communication skill than the boys in this group.

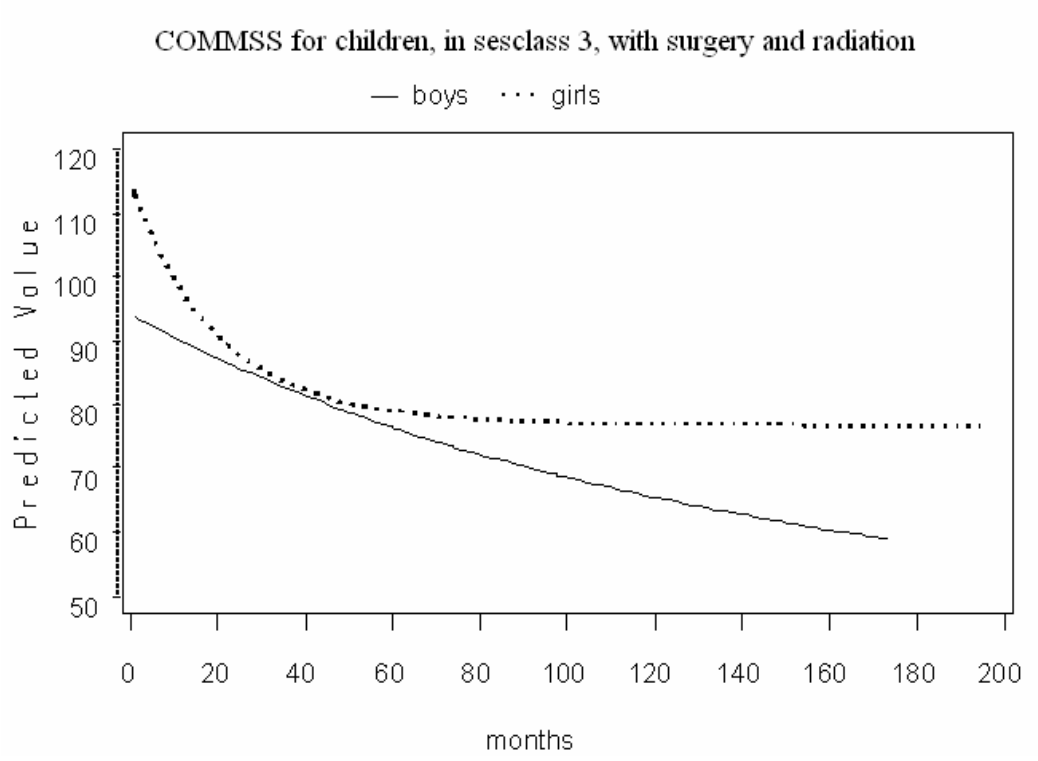

Figure 4.6. Curves of communication standard scores for children who are in SES class 3 and with treatments of surgery and radiation.

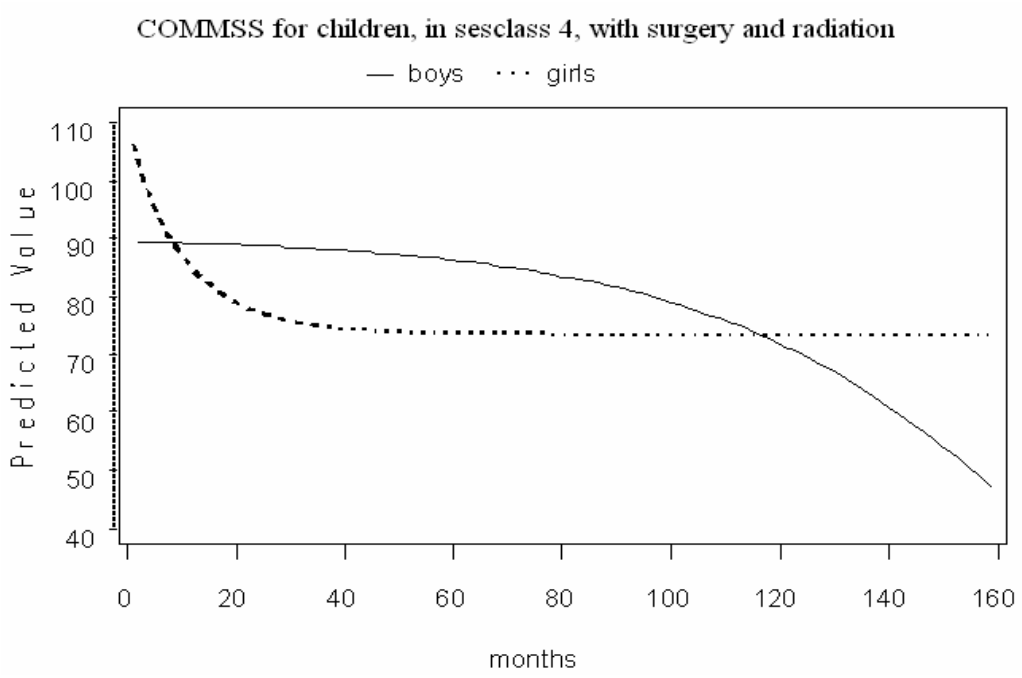

Figure 4.7. Curves of communication standard scores for children who are in SES class 4 and with treatments of surgery and radiation.

Figure 4.7 shows the comparison of communication skills of boys and girls who are in SES class 4 and had taken surgery and radiation. In this group, there are 11 patients and 51 observations for boys and 11 patients and 48 observations for girls. In this figure, the curve for boys falls sharply after 6 years. On the other hand, the curve for girls falls sharply in the first two years, and then it turns flat. In this group, shapes of the curves between boys and girls seem to be different. It may be caused by the small sample sizes.

Based on the above comparison analysis on gender for communication skill, it seems that girls performed better in communication skill with higher SES classes than that of boys.

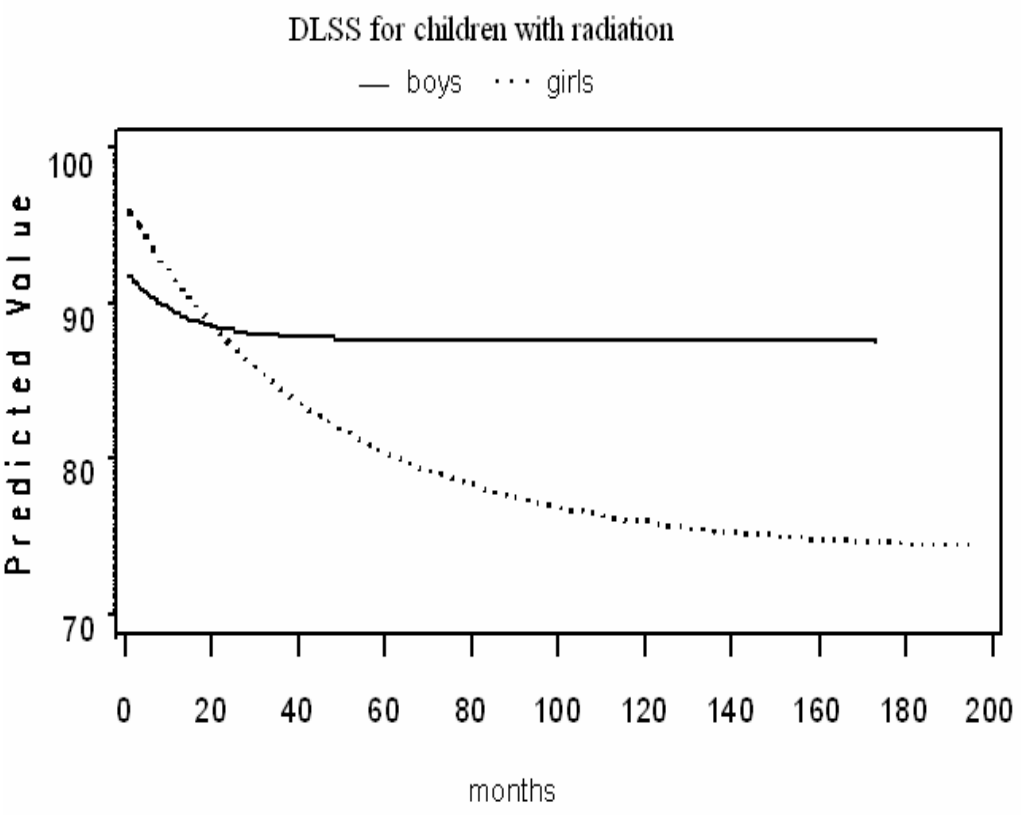

Figure 4.8. Curves of daily living skills standard scores for children with treatment of radiation.

Figure 4.8 and figure 4.9 show the curves of standard scores of daily living skills for boys and girls with radiation and without radiation, respectively. In the group with radiation, there are 36 patients and 108 observations for boys and 33 patients and 129 observations for girls. In the group without radiation, there are 26 patients and 110 observations for boys and 23 patients and 109 observations for girls. In figure 4.8, curve of boys goes down more slowly than that of girls in first two years. The curve for boys becomes flat, while that for girls keeps on falling. In Figure 4.9, both the curve of boys and the curve of girls go up in a similar rate in the first year. After one year both curves

become flat. So for daily living skills, girls seem to have more problems with radiation than boys.

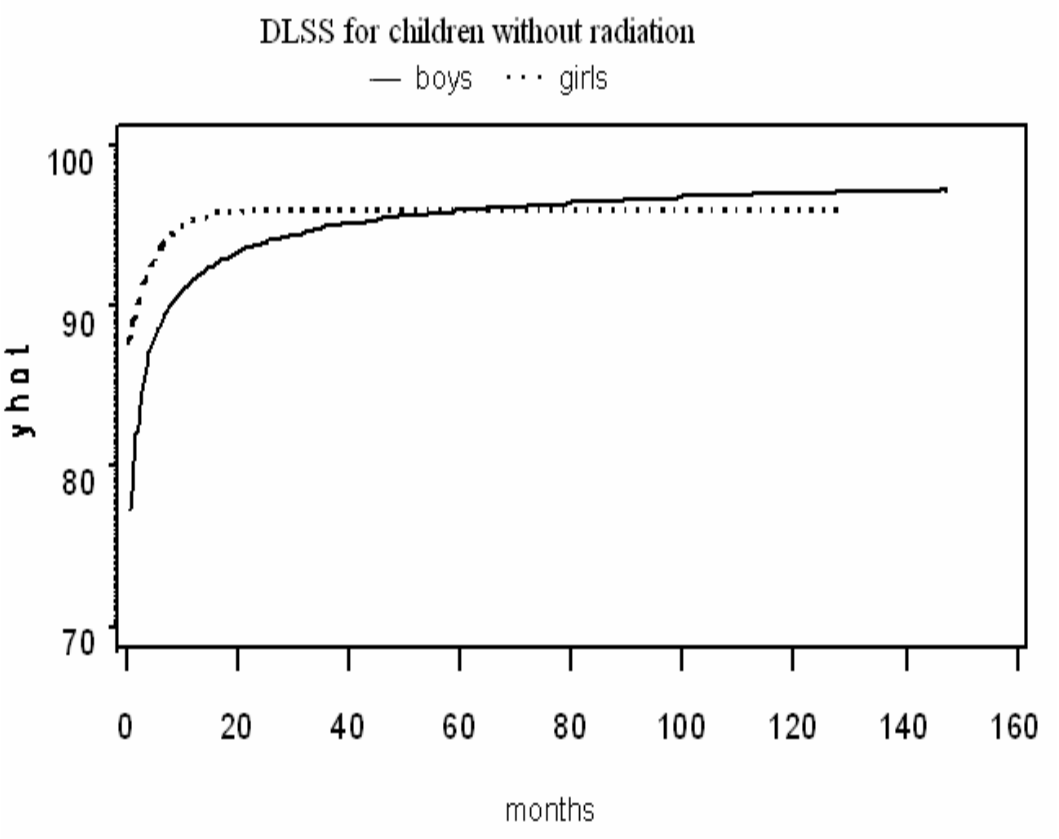

Figure 4.9 Curves of daily living skills standard scores for children with treatment of non-radiation

4.3 Comparison between radiation and non-radiation

There are five graphics that show the comparison of effect between radiation and non-radiation. Figure 4.10 to figure 4.12 are about the communication skill. Figure 4.13 and figure 4.14 are regarding to daily living skills.

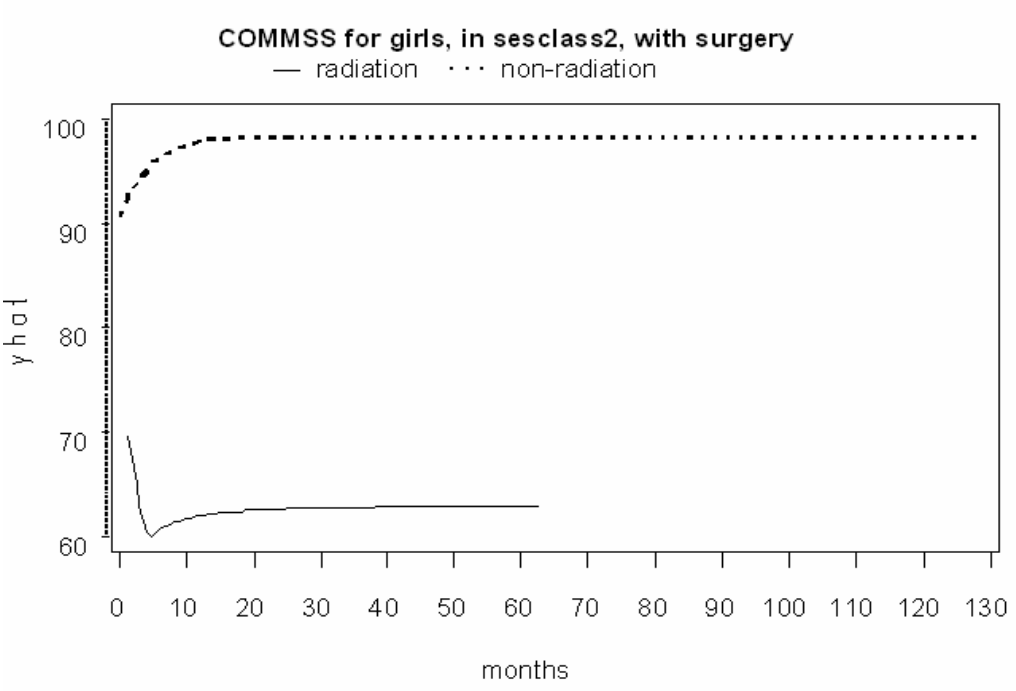

Figure 4.10. Curves of communication standard scores for girls who are in SES class 2 and with surgery

Figure 4.10 shows the comparison between radiation and non-radiation for the group of girls who are in SES class 2 with surgery. In this group, there are 4 patients and 13 observations for radiation and 9 patients 49 observations for non-radiation. Curve of radiation falls in the first five months and then becomes flat. Curve of non-radiation goes up in the first year and then becomes flat. In this group, it is very clear that non-radiation patients outperform those of radiation in communication skill. It remains uncertain that the cause of this fact is due to radiation or due to the patients with radiation had more serious tumor at the beginning.

Figure 4.11 shows the comparison in the group of boys who are in SES class 3 with surgery. In this group, there are 8 patients and 51 observations for radiation and 8

patients and 30 observations for non-radiation. Radiation patients seem to drop quickly to the level of non-radiation patients after 7 years. Combining this graph with figure 4.10, we see the radiation boys were outperformed by the non-radiation boys in either low or high SES class. Again as we mentioned before, this fact may indicate the negative impact of the radiation. However, the impact could come from the fact that the radiation boys had worse tumor condition than non-radiation boys in the sample. Further studies may be necessary to answer this question

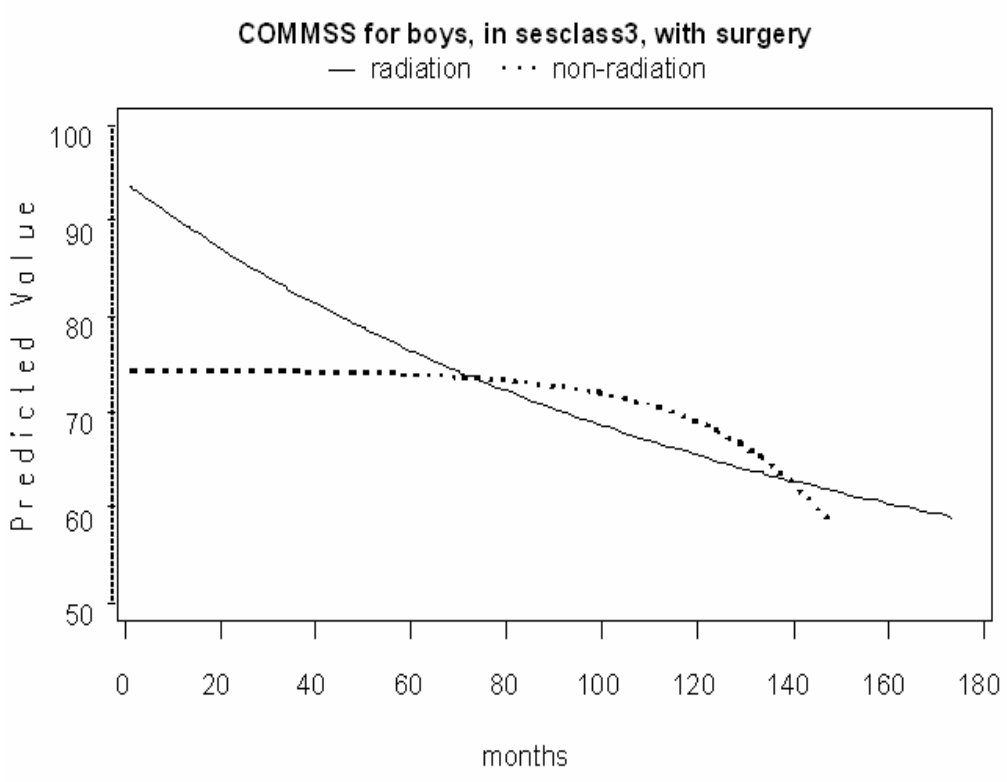

Figure 4.11. Curves of communication standard scores for boys who are in SES class 3 and with surgery.

Figure 4.12 shows the comparison of communication skills between radiation and non-radiation in the group of girls who are in SES class 4 with surgery. In this group, there are 11 patients and 48 observations for radiation and 5 patients and 24

observations for non-radiation. The curve of radiation falls sharply in first two years, and clearly worse than that of non-radiation.

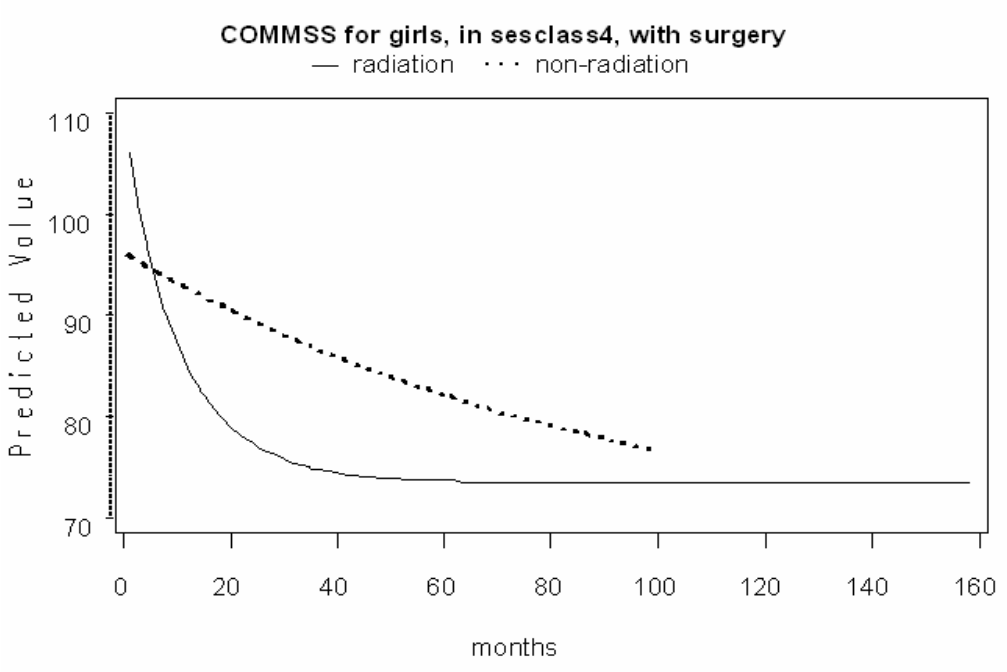

Figure 4.12. Curves of communication standard scores for girls who are in SES class 4 and with surgery.

From the above comparison analysis on radiation or not for communication skill, we can see that different results show up for different groups. The interactions among these factors are obvious.

For daily living skills, next two graphs, figure 4.13 and figure 4.14, show the comparison between radiation and non-radiation. Figure 4.13 shows the comparison in girls. In this group, there are 33 patients and 129 observations for radiation and 23 patients and 109 observations for non-radiations. The curve of girls with radiation goes down quickly in the first 8 years, and becomes flat after that. The curve of girls without

radiation remains flat except the first year. In this group, girls without radiation have much better performance on daily living skills than girls with radiation.

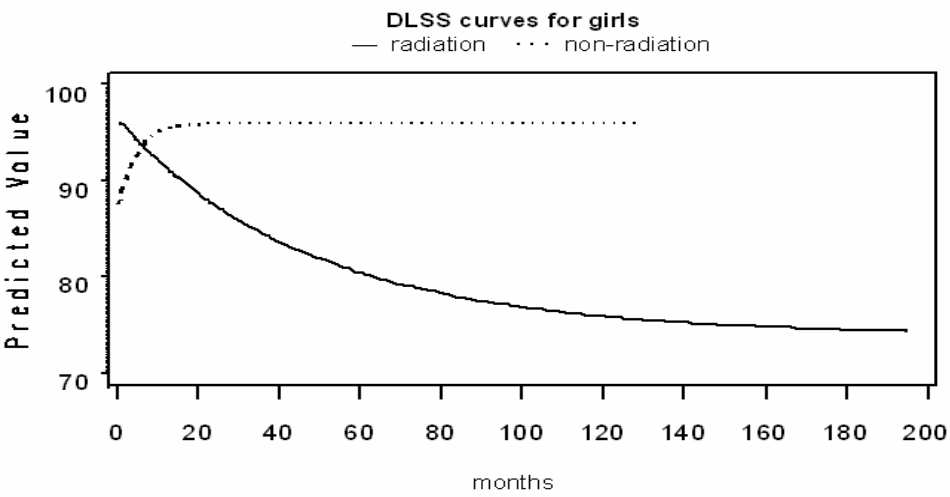

Figure 4.13. Curves of standard scores of daily living skills for girls with or without radiation.

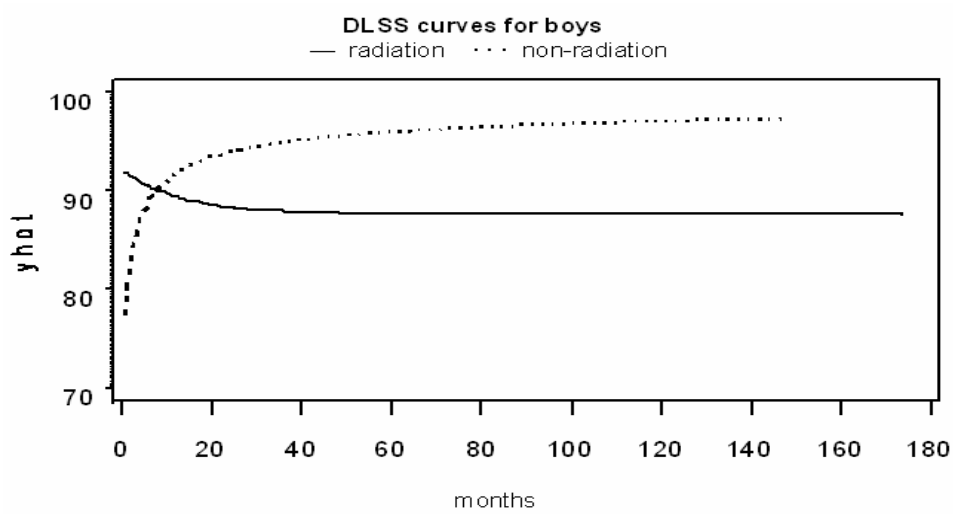

Figure 4.14. Curves of standard scores of daily living skills for boys with or without radiation.

Figure 4.14 shows the comparison in boys. In this group, there are 36 patients and 180 observations for radiation and 26 patients and 110 observations for non-radiation. The pattern of trajectories for boys is similar to the group of girls. Again, boys without radiation have better performance on daily living skills than boys with radiation.

Based on the above comparison analysis on radiation for daily living skills, it can be concluded that children without radiation performed better on daily living skills than those with radiation.

Chapter Five: Conclusion and Future Research

This study examined change in adaptive outcomes of children who are treated for brain tumor. There has been little work on change in outcomes overtime using a prospective longitudinal research design. Statistic methods in most research on cognitive outcome are linear models. Fractional polynomial transformation method is a popular method in many cases of model building procedures. Gompertz method has been applied widely on actuarial science. Gompertz curve is also used as growth curve in many fields, such as baby's growth curve [3]. We apply fractional polynomial transformation and Gompertz method on building non-linear models for longitudinal curves in this thesis. They provided reasonably good fit. In this thesis, Gompertz method gives the better fit than Fractional polynomial transformation method in most cases.

One of the results we found was that radiation treatment produces worse adaptive outcomes, especially for communication skill and daily living skills. This result consists with one of side effects of radiation therapy - the neurological effects most affecting quality of life are eventual permanent memory and speech problems [12].

Since many factors impact the outcomes of Vineland Scores, to study the trajectories of the scores requires large number of observations for each combination of factors. Therefore, a larger sample size maybe needed for more sophisticated statistical analyses and greater statistical power.

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[13] Brainscience Foundation, http://www.brainsciencefoundation.org/.

[14] Brain & Neuro Surgery Information center – brain tumor in children, http://www.brain-surgery.com/chtum2.html/.

Appendix A: SAS Code for Mixed model

```
/* Significant variables for communication skill standard scores */
proc mixed data=tmp1.all;
        class sex trt1 trt2 trt3 sesclass;
        model commss=months_between agedxy sex trt1 trt2 trt3 sesclass
        agedxy*months_between trt1*months_between trt2*months_between
        trt3*months_between sex*months_between sesclass*months_between
        agedxy*sex trt1*sex trt2*sex trt3*sex sesclass*sex/solution;
        repeated/type=cs subject=idnum;
        title 'model with communication total standard score';
run;
/* Significant variables for daily living skills standard scores */
proc mixed data=tmp1.all;
        class sex trt1 trt2 trt3 sesclass;
        model dlss=months_between agedxy sex trt1 trt2 trt3 sesclass
        agedxy*months_between trt1*months_between trt2*months_between
        trt3*months_between sex*months_between sesclass*months_between
        agedxy*sex trt1*sex trt2*sex trt3*sex sesclass*sex/solution;
        repeated/type=cs subject=idnum;
        title 'model with daily living total standard score';
run;
/* Significant variables for socialization skill standard scores */
proc mixed data=tmp1.all;
```

```
        class sex trt1 trt2 trt3 sesclass;
        model socss=months_between agedxy sex trt1 trt2 trt3 sesclass
        agedxy*months_between trt1*months_between trt2*months_between
        trt3*months_between sex*months_between sesclass*months_between
        agedxy*sex trt1*sex trt2*sex trt3*sex sesclass*sex/solution;
        repeated/type=cs subject=idnum;
        title 'model with socialization total standard score';
run;
```

Appendix B: SAS Code for Fitting Longitudinal Curves

B.1 Transformation method

```
/* MACRO code for transformation*/
/* doing transformation to two factors, in which both powers are not zero; */
%macro trans(dataset=);
%let n=0;
%do i=1 %to 11;
%do j=&i %to 11;
%let n=%sysevalf(&n+1.0);
%let ci=%sysevalf(-2.5+&i*0.5);
%let cj=%sysevalf(-2.5+&j*0.5);
        %if %sysevalf(&ci=&cj and &ci^=0 and &cj^=0) %then
                %do;
                        data out;
```

```
                    set &dataset;
                    f1=months_between**(&ci);
                    f2=f1*(log(months_between));
        %end;
%if %sysevalf(&ci^=&cj and &ci^=0 and &cj^=0) %then
        %do;
            data out;
                    set &dataset;
                    f1=months_between**%sysevalf(&ci);
                    f2=months_between**%sysevalf(&cj);
        %end;

proc mixed data=out;
        ods output fitstatistics=fs;
        model dlraw=f1 f2;
        repeated/type=cs subject=idnum;
        title "model &ci and &cj ";
run;
data fs&n;
        set fs;
        p1=&ci;
        p2=&cj;
        if p1=0 then
```

```
                do;
                        descr='.';
                        value=.;
                        p1=.;
                        p2=.;
            end;
        if _n_=1 then output fs&n;
        run;

%end;
%end;
%mend trans;

/* doing transformation to two factors in which at least one power is 0;*/
%macro trans2(dataset=);
%let n=0;
%do i=1 %to 11;
%let n=%sysevalf(&n+1.0);
%let ci=%sysevalf(-2.5+&i*0.5);
    %if %sysevalf(&ci=0) %then
        %do;
                data out;
                        set &dataset;
```

```
                    f1=log(months_between);
                    f2=(log(months_between)**2);
        %end;

%else
        %do;
                data out;
                    set &dataset;
                    f1=months_between**&ci;
            f2=log(months_between);
                run;
        %end;
proc mixed data=out;
        ods output fitstatistics=fs;
        model dlraw=f1 f2;
        repeated/type=cs subject=idnum;
        title "model &ci and 0 ";
run;
data f2s&n;
        set fs;
        p1=&ci;
        p2=0;
        if _n_=1 then output f2s&n;
```

```
        run;
%end;
%mend trans2;

/* doing transformation to single factor; */
%macro trans1(dataset=);
%let n=0;
%do i=1 %to 11;
%let n=%sysevalf(&n+1.0);
%let ci=%sysevalf(-2.5+&i*0.5);
        %if %sysevalf(&ci=0) %then
                %do;
                        data out;
                                set &dataset;
                                f1=log(months_between);
                %end;
        %else
                %do;
                        data out;
                                set &dataset;
                                f1=months_between**%sysevalf(&ci);
                %end;
        proc mixed data=out;
```

```
            ods output fitstatistics=fs;
            model dlraw=f1;
            repeated/type=cs subject=idnum;
            title "model &ci";
        run;
            quit;
        data f1s&n;
            set fs;
            p1=&ci;
            p2=.;
            if _n_=1 then output f1s&n;
        run;
%end;
%mend trans1;

%macro merge;
%let name=fs1;
%do i=2 %to 66;
%let name=&name fs&i;
%end;
%do i=1 %to 11;
%let name=&name f2s&i;
%end;
```

```
%do i=1 %to 11;
%let name=&name f1s&i;
%end;
data one;
set &name;
if descr='.' then delete;
run;
%mend merge;

/* transformation method for fitting longitudinal curve for boys who are in SES class 2
with surgery and no radiation */
proc sql;
create table c as
select idnum, commss, months_between,sesclass, sex,trt1,trt3
from tmp1.all
where sesclass=2 and trt1=0 and sex=1 and trt3=1;
quit;
%trans(dataset=c);
%trans2(dataset=c);
%trans1(dataset=c);
%merge;
proc sort data=one;
by value;
```

```
run;
proc mixed data=c;
model commss=months_between/solution;
repeated/type=cs subject=idnum;
title 'linear model';
run;
data ct;
        set c;
        f1=months_between**(-2);
        f2=months_between**(-1.5);
run;
proc mixed data=ct;
        ods output Influence=pressR;
        model commss=f1 f2/solution influence;
        repeated/type=cs subject=idnum;
run;
data tmp1.coms_sc2_m_s_nr_trs;
        set ct;
        yhat= 90.5238 -70.2713*f1+73.1317*f2;
        run;
symbol1 color=black i=none v=star ;
symbol2 color=black i=splines v=none;
axis1 label=(r=0 a=90);
```

```
title1 ;
title2 'Commss curve for(sesclass2, surgery, male, nonradiation)';
title3 "-Transformation Method";

proc gplot data= tmp1.coms_sc2_m_s_nr_trs;
        plot dlss*months_between=1 yhat*months_between=2/vaxis=axis1 vminor=50
        hminor=0 overlay;
        title ;
run;
quit;
proc sql;
select sum(pressres**2)as press
from pressr;
quit;

/* transformation method for fitting longitudinal curve for boys who are in SES class 3
with surgery and radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass, sex, trt1,trt3
from tmp1.all
where sesclass=3 and trt1=0 and sex=1 and trt3=0;
quit;
```

```
%trans(dataset=c);

%trans2(dataset=c);

%trans1(dataset=c);

%merge;

proc sort data=one;

by value;

run;

proc mixed data=c;

model commss=months_between/solution;

repeated/type=cs subject=idnum;

title 'linear model';

run;

data ct;

        set c;

        f1=months_between**(-0.5);

        f2=f1*(log(months_between));

proc mixed data=ct;

        ods output Influence=pressR;

        model commss=f1 f2/solution influence;

        repeated/type=cs subject=idnum;

run;

data tmp1.coms_sc3_m_s_r_trs;

        set ct;
```

```
        yhat=    28.2386 + 44.9219*f1+ 76.1274*f2;
        run;
symbol1 color=black i=none v=star ;
symbol2 color=red i=splines v=star;
axis1 label=(r=0 a=90);
title1 ;
title2 'Commss curve for group (sesclass3, surgery, male, radiation)';
title3 " -Transformation Method";
proc gplot data= tmp1.coms_sc3_m_s_r_trs;
        plot commss*months_between=1 yhat*months_between=2/vaxis=axis1
        vminor=50 hminor=0 overlay;
run;
quit;
proc sql;
select sum(pressres**2)as press
from pressr;
quit;


/* transformation method for fitting longitudinal curve for girls who are in SES class 4
with surgery and radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass, sex, trt1,trt3
```

```
from tmp1.all
where sesclass=4 and trt1=0 and sex=2 and trt3=0;
quit;
%trans(dataset=c);
%trans2(dataset=c);
%trans1(dataset=c);
%merge;
proc sort data=one;
by value;
run;
proc mixed data=c;
model commss=months_between/solution;
repeated/type=cs subject=idnum;
title 'linear model';
run;
data ct;
        set c;
        f1=months_between**(-1.5);
        f2=months_between**(-1);
proc mixed data=ct;
        ods output Influence=pressR;
        model commss=f1 f2/solution influence;
        repeated/type=cs subject=idnum;
```

```
        title ;
        run;
data tmp1.coms_sc4_f_s_r_trs;
        set ct;
        yhat=  71.3198 -165.07*f1+ 190.10*f2;
        run;
symbol1 color=black i=none v=star ;
symbol2 color=red i=splines v=star;
axis1 label=(r=0 a=90);
title1 ;
title2 'Commss curve for group (sesclass4, surgery, female, radiation)';
title3 " -Transformation Method";
proc gplot data= tmp1.coms_sc4_f_s_r_trs;
        plot commss*months_between=1 yhat*months_between=2/vaxis=axis1
vminor=50 hminor=0 overlay;
        title ;
run;
quit;
proc sql;
select sum(pressres**2)as press
from pressr;
quit;
```

```
/* transformation method for fitting longitudinal curve for girls who are in SES class 4
with surgery and no radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass, sex, trt1,trt3
from tmp1.all
where sesclass=4 and trt1=0 and sex=2 and trt3=1;
quit;
%trans(dataset=c);
%trans2(dataset=c);
%trans1(dataset=c);
%merge;
proc sort data=one;
by value;
run;
proc mixed data=c;
model commss=months_between/solution;
repeated/type=cs subject=idnum;
title 'linear model';
run;
data ct;
        set c;
        f1=months_between**(-0.5);
```

```
        f2=months_between**(-1);
proc mixed data=ct;
        ods output Influence=pressR;
        model commss=f1 f2/solution influence;
        repeated/type=cs subject=idnum;
        title ;
        run;
data tmp1.coms_sc4_f_s_nr_trs;
        set ct;
        yhat= 76.4980 +60.2018*f1 -36.5616*f2;
        run;
symbol1 color=black i=none v=star ;
symbol2 color=red i=splines v=star;
axis1 label=(r=0 a=90);
title1 ;
title2 'Commss curve for group (sesclass4, surgery, female, nonradiation)';
title3 " -Transformation Method";
proc gplot data= tmp1.coms_sc4_f_s_nr_trs;
        plot commss*months_between=1 yhat*months_between=2/vaxis=axis1
vminor=50 hminor=0 overlay;
        title ;
run;
quit;
```

```
proc sql;
select sum(pressres**2)as press
from pressr;
quit;

/* transformation method for fitting longitudinal curve of daily living skills for boys
with radiation */
proc sql;
create table c as
select idnum, dlss, months_between, sex,trt3
from tmp1.all
where sex=1 and trt3=0;
quit;
%trans(dataset=c);
%trans2(dataset=c);
%trans1(dataset=c);
%merge;
proc sort data=one;
by value;
run;
proc mixed data=c;
model dlss=months_between/solution;
repeated/type=cs subject=idnum;
```

```
title 'linear model';
run;
data ct;
        set c;
        f1=months_between**(-1.5);
        f2=months_between**(-2);
proc mixed data=ct;
        ods output Influence=pressR;
        model dlss=f1 f2/solution influence;
        repeated/type=cs subject=idnum;
        title ;
        run;
data tmp1.ds_m_r_trs;
        set ct;
        yhat=  87.8445+52.8074*f1  -50.1841*f2;
        run;
symbol1 color=black i=none v=star ;
symbol2 color=red i=splines v=star;
axis1 label=(r=0 a=90);
title1 ;
title2 "Dlss growth curve for group (male, radiation)";
title3 "-Transformation Method";
proc gplot data= tmp1.ds_m_r_trs;
```

```
        plot dlss*months_between=1 yhat*months_between=2/vaxis=axis1 vminor=50
hminor=0 overlay;
run;
quit;
proc sql;
select sum(pressres**2)as press
from pressr;
quit;


/* transformation method for fitting longitudinal curve of daily living skills for boys
without radiation */
proc sql;
create table c as
select idnum, dlss, months_between, sex,trt3
from tmp1.all
where sex=1 and trt3=1;
quit;
%trans(dataset=c);
%trans2(dataset=c);
%trans1(dataset=c);
%merge;
proc sort data=one;
```

```
by value;
run;
proc mixed data=c;
model dlss=months_between/solution;
repeated/type=cs subject=idnum;
title 'linear model';
run;
data ct;
        set c;
        f1=months_between**(-0.5);
        f2=months_between**(-1);
proc mixed data=ct;
        ods output Influence=pressR;
        model dlss=f1 f2/solution influence;
        repeated/type=cs subject=idnum;
        title ;
        run;
data tmp1_ds_m_nr_trs;
        set ct;
        yhat=  99.7346 -30.3621*f1+ 9.5250*f2;
        run;
symbol1 color=black i=none v=dot ;
symbol2 color=black i=splines v=none l=1;
```

```
axis1 label=(r=0 a=90);

title1 ;

title2 "Dlss growth curve for group (male, nonradiation)";

title3 "-Transformation Method";

proc gplot data= tmp1_ds_m_nr_trs;

        plot dlss*months_between=1 yhat*months_between=2/vaxis=axis1 vminor=50

hminor=0 overlay;

run;

quit;

proc sql;

select sum(pressres**2)as press

from pressr;

quit;
```

B.2 Gompertz method

```
/* Gompertzt method for fitting longitudinal curve for boys who are in SES class 2 with

surgery and no radiation */

proc nlmixed data=c;

parms

a0=90

b0=-3.2

b1=-0.04
```

```
s2u1=100

s2e=100;

a0ind=a0+u1;

*prediction;

yhat=a0*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

yhaty=a0ind*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

*model statement;

model commss~normal(yhaty,s2e);

random u1~normal(0,s2u1) subject=idnum;

predict yhat out= tmp1.coms_sc2_m_s_nr_gpz;

run;

symbol1 color=black i=none v=star ;

symbol2 color=black i=splines v=none;

axis1 label=(r=0 a=90);

title1 ;

title2 'Commss curve for(sesclass2, surgery, male, nonradiation)';

title3 " -Gompertz Method";

proc gplot data= tmp1.coms_sc2_m_s_nr_gpz;

plot commss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50

hminor=0 overlay;

title ;

run;

quit;
```

```
data cp;
set c;
n=_n_;
run;
proc sql;
select count(commss) as m
from c;
quit;

/* Gompertz method for fitting longitudinal curve for boys who are in SES class 3 with
surgery and radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass, sex, trt1,trt3
from tmp1.all
where sesclass=3 and trt1=0 and sex=1 and trt3=0;
quit;
proc nlmixed data=c;
parms
a0=95
b0=-10
b1=-0.001
s2u1=50
```

```
s2e=100;

a0ind=a0+u1;

*prediction;

yhat=a0*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

yhaty=a0ind*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

*model statement;

model commss~normal(yhaty,s2e);

random u1~normal(0,s2u1) subject=idnum;

predict yhat out= tmp1.coms_sc3_m_s_r_gpz;

run;

symbol1 color=black i=none v=star ;

symbol2 color=red i=splines v=star;

axis1 label=(r=0 a=90);

title1 ;

title2 'Commss curve for group (sesclass3, surgery, male, radiation)';

title3 " -Gompertz Method";

proc gplot data= tmp1.coms_sc3_m_s_r_gpz;

plot commss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50

hminor=0 overlay;

title ;

run;

quit;
```

```
/* Gompertzt method for fitting longitudinal curve for girls who are in SES class 4 with
surgery and radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass, sex, trt1,trt3
from tmp1.all
where sesclass=4 and trt1=0 and sex=2 and trt3=0;
quit;
proc nlmixed data=c;
parms
a0=95
b0=-1
b1=0.1
s2u1=100
s2e=100;
a0ind=a0+u1;
*prediction;
yhat=a0*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));
yhaty=a0ind*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));
*model statement;
model commss~normal(yhaty,s2e);
random u1~normal(0,s2u1) subject=idnum;
predict yhat out= tmp1.coms_sc4_f_s_r_gpz;
```

```
run;
symbol1 color=black i=none v=star ;
symbol2 color=red i=splines v=star;
axis1 label=(r=0 a=90);
title1 ;
title2 'Commss curve for group (sesclass4, surgery, female, radiation)';
title3 " -Gompertz Method";
proc gplot data= tmp1.coms_sc4_f_s_r_gpz;
plot commss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50
hminor=0 overlay;
run;
quit;

/* Gompertzt method for fitting longitudinal curve for girls who are in SES class 4 with
surgery and no radiation */
proc sql;
create table c as
select idnum, commss, months_between, sesclass,sex, trt1,trt3
from tmp1.all
where sesclass=4 and trt1=0 and sex=2 and trt3=1;
quit;
proc nlmixed data=c;
parms
```

```
a0=105

b0=-10

b1=-0.01

s2u1=10

s2e=100;

a0ind=a0+u1;

*prediction;

yhat=a0*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

yhaty=a0ind*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));

*model statement;

model commss~normal(yhaty,s2e);

random u1~normal(0,s2u1) subject=idnum;

predict yhat out= tmp1.coms_sc4_f_s_nr_gpz;

title ;

run;

symbol1 color=black i=none v=star ;

symbol2 color=red i=splines v=star;

axis1 label=(r=0 a=90);

title1 ;

title2 'Commss curve for group (sesclass4, surgery, female, nonradiation)';

title3 " -Gompertz Method";

proc gplot data= tmp1.coms_sc4_f_s_nr_gpz;
```

```
plot commss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50
hminor=0 overlay;
run;
quit;


/* Gompertzt method method for fitting longitudinal curve of daily living skills for boys
with radiation */
proc sql;
create table c as
select idnum, dlss, months_between, sex,trt3
from tmp1.all
where sex=1 and trt3=0;
quit;
title1 ;
title2 "Dlss growth curve for group (male, radiation)";
proc nlmixed data=c;
parms
a0=95
b0=-10
b1=-0.1
s2u1=200
s2e=200;
```

```
a0ind=a0+u1;
*prediction;
yhat=a0*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));
yhaty=a0ind*exp(-(exp(b0)*(exp(b1*months_between)-1)/b1));
*model statement;
model dlss~normal(yhaty,s2e);
random u1~normal(0,s2u1) subject=idnum;
predict yhat out=tmp1.ds_m_r_gpz;
title ;
run;
title1 ;
title2 "Dlss growth curve for group (male, radiation)";
title3 "-Gompertz Method";
proc gplot data= tmp1.ds_m_r_gpz;
plot dlss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50
hminor=0 overlay;
run;
quit;

/* Gompertzt method method for fitting longitudinal curve of daily living skills for boys
without radiation */
proc sql;
create table c as
```

```
select idnum, dlss, months_between, sex,trt3
from tmp1.all
where sex=1 and trt3=1;
quit;
proc nlmixed data=c;
parms
a0=95
b0=-10
b1=-0.1
s2u1=200
s2e=200;
a0ind=a0+u1;
*prediction;
yhat=a0*exp((exp(b0)*(exp(b1*months_between)-1)/b1));
yhaty=a0ind*exp((exp(b0)*(exp(b1*months_between)-1)/b1));
*model statement;
model dlss~normal(yhaty,s2e);
random u1~normal(0,s2u1) subject=idnum;
predict yhat out= tmp1.ds_m_nr_gpz;
title ;
run;
title1 ;
title2 "Dlss growth curve for group (male, nonradiation)";
```

```
proc gplot data= tmp1.ds_m_nr_gpz;
plot dlss*months_between=1 pred*months_between=2/vaxis=axis1  vminor=50
hminor=0 overlay;
title3 "-Gompertz Method";
run;
quit;
```

Appendix C: SAS Code for Calculation of PRESS of Gompertz method

```
%macro gompress(data=,m=, y=);
%do i=1 %to &m;
        data d&i;
        set &data;
        if _n_=&i then dlraw=.;
        proc nlmixed data=d&i;
                parms
                        a0=80
                        b0=-5
                        b1=-0.01
                        s2u1=200
                        s2e=200;
                        a0ind=a0+u1;
                *prediction;
                yhat=a0*exp((exp(b0)*(exp(b1*months_between)-1)/b1));
```

```
            yhaty=a0ind*exp((exp(b0)*(exp(b1*months_between)-1)/b1));
            *model statement;
            model dlraw~normal(yhaty,s2e);
            random u1~normal(0,s2u1) subject=idnum;
            predict yhat out=o&i;
        run;
        proc sql;
            create table p&i as
            select a.&y-b.pred as pr
            from &data a, o&i b
            where a.n=b.n=&i;
        quit;
%end;
%mend gompress;


%macro press(m=);
        %let name=p1;
        %do i=2 %to &m;
        %let name=&name p&i;
        %end;
        data pp;
            set &name;
        run;
```

```
    proc sql;
        select sum(pr**2) as press
        from pp;
    quit;
%mend press;
```