Comparison of different weight growth models in a sample of children from 6 to 15 years

Neha Wadhawan

A Thesis

in

the Department

of

Mathematics and Statistics

Presented in Partial Fulfillment of the Requirements

for the degree of Master of Arts (Mathematics) at

Concordia University

Montreal, Quebec, Canada

September, 2018

CONCORDIA UNIVERSITY

School of Graduate Studies

This is to certify that the thesis prepared

By: **Neha Wadhawan**

Entitled: **Comparison of different weight growth models in a sample of children from 6 to 15 years**

and submitted in partial fulfillment of the requirements for the degree of

Master of Arts (Mathematics)

complies with the rules and regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the final examining committee:

____________________________ Chair
Dr. Cody Hyndman

____________________________ Examiner
Dr. Arusharka Sen

____________________________ Examiner
Dr. Debaraj Sen

____________________________ Thesis Supervisor
Dr. Lisa Kakinami

____________________________ Thesis Co-Supervisor
Dr. Yogendra Chaubey

Approved by ____________________________
Dr. Arusharka Sen, Graduate Program Director

September 19, 2018 ____________________________
Date Dr. André Roy, Dean, Faculty of Arts and Science

ABSTRACT

Comparison of different weight growth models in a sample of children from 6 to 15 years

Neha Wadhawan

Human growth is a complex, natural developmental phenomenon comprised of prenatal (fetal) and postnatal (infancy, childhood, adolescence, and adulthood) growth. Weight is an eco-sensitive growth measurement that responds more rapidly to illness and loss of appetite than height. Modelling postnatal growth in children's weight is of particular interest in order to identify those at greatest risk for serious health outcomes later in adult life such as obesity, hypertension, cardiovascular disease, and diabetes. Traditionally, the most commonly used parametric growth models (Jenss-Bayley, Reed 1^{st} order and Reed 2^{nd} order) have been recommended for children from birth to 6 years of age but the literature on their performance in an older age range of children is limited. The Adapted Jenss-Bayley was developed to extend the models from birth to puberty. In contrast, the recently developed SITAR (SuperImposition by Translation And Rotation) model has no age range constraints, and has been shown to be superior to the previous models (Jenss-Bayley and Reed 1^{st} order) for modeling weight from birth to four years of age. No study has yet assessed the comparison and performance of these models in an older age range of children. This present study aims to extend the previous work by comparing these models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, Adapted Jenss-Bayley, and SITAR) within the mixed effect framework to model longitudinal weight in an age range of children that starts from middle childhood and includes puberty (6 to 15 years) in the Quebec Longitudinal Study of Child Development (QLSCD) cohort ($n = 2,120$). Results demonstrate that the SITAR model outperformed the other four models but should be reassessed in additional studies with longer follow-up.

Acknowledgement

I would first like to express my warmest gratitude to both my supervisors Dr. Yogendra Chaubey and Dr. Lisa Kakinami for their immense support, motivation, and valuable guidance throughout my Master's program at Concordia University. Whatever may be the situation, both of them have always been there as a guide and a true mentor. Their expertise, understanding and patience has added considerably to my graduate experience. I would not have considered a graduate career in applied statistics without their belief and encouragement.

A very special thanks goes to my supervisor, Dr. Lisa Kakinami for making this research a truly incredible learning and growth experience. Her vast knowledge in Epidemiology, immensely helped in completing this research work. She was always available whenever I needed her guidance. Her valuable comments and reviews has helped me in developing this thesis to its present state.

I would also like to thank my thesis committee Dr. Arusharka Sen and Dr. Debaraj Sen for reviewing my thesis. My sincere regards goes out to all the professors of the Mathematics and Statistics Department who have greatly helped in enhancing my knowledge in Statistics. Also, I would like to offer my special thanks to the entire administrative staff of Mathematics and Statistics Department for their consistent assistance and support throughout the program.

Finally, I would like to thank my husband Abhishek Sood for his great support, love, managing all the household errands and taking very good care of our daughter while I was busy with my studies. Also, a very special thanks to my little girl Anaya Wadhawan Sood for being such a supportive kid. You are my rock! I must express my very profound gratitude to my parents (Bina Wadhawan and Suraj Wadhawan) and my sister (Meghna Wadhawan) for providing me with consistent support, love and inspiration throughout my life. This accomplishment would not have been possible without all of them.

Thank you once again to all the wonderful people!

Contents

List of Tables

List of Figures

Chapter 1

Introduction

1.1 Background

Human physical growth is a complex, natural developmental phenomenon (Haralabakis & Spyropoulou, 1990). In the literature, it is defined as a quantitative progressive increase in the physical size or mass and shape of the body as a whole and of its parts over a period of time occurring between conception and full maturation (Tanner, 1990; Hauspie, Cameron, Molinari, & MyiLibrary, 2004; Malina, 2012). The overall human growth process is generally divided into two life phases: Prenatal growth and Postnatal growth (Tanner, 1990).

Prenatal growth - Prenatal development refers to the process in which a baby develops from a single cell after conception into an embryo and later as a fetus. This phase is characterized by a rapid increase in cell numbers and fast growth rates. The prenatal development starts on the date of conception, and takes about 38 weeks to complete.

Postnatal growth – The postnatal growth process starts after the birth of a child. It is defined as a smooth continuous process through which the child grows and matures from birth to adulthood. It is further generally divided into five stages: namely neonatal (birth to 1 month), infancy (early: 1 to 6 months, later: 6 months to 2 years), childhood (early: 2 to 5 years, middle: 5 to 8 years or later: 9 to 11 years), adolescence (approximately 11 or 12 years to 18 years) and adulthood (18 years and older) (Ellis, 1951; Balaban & Bobick, 2008). For the purposes of this thesis, postnatal weight development will be focused on exclusively, and prenatal growth will not be further considered.

The overall human growth process involves the growing of different body parts at different growth rates and at different times (Malina, 2012). In order to determine how healthy the child is growing postnatally, their height and weight are measured over time (Silverwood, 2008; Malina, 2012). Historically, the height of a child has been the main center of focus in research. Indeed several previous studies primarily focused on developing mathematical growth models for the appropriate modelling of a child's height from birth or infancy to adulthood (Bock & Thissen, 1976; Preece & Baines, 1978; Karlberg, 1987; Jolicoeur, Pontier, Pernin, & Sempé, 1988). In contrast, much less is known about the weight development of a child as only a few researchers have focused on modelling children's postnatal weight (Jenss & Bayley, 1937; Count, 1943; Berkey & Reed, 1987).

The most helpful tools that are often utilized in order to study the human growth process over time are the distance curve, velocity curve, and acceleration curve (Hauspie et al., 2004). The distance curve is defined as the amount of growth attained or measured at each age (Bogin, 2015). On the other hand, the velocity curve is defined as the increase in growth measurement at each age (Bogin, 2015). The acceleration curve is difficult to interpret, and the distance curve has been criticized for providing too little information. Thus the velocity curve is the most commonly utilized in research (Hauspie et al., 2004). However, the velocity curve and acceleration curve can be easily obtained from first and second differentiations of the distance curve respectively. The acceleration curve can also be obtained by taking the first derivative of the velocity curve. The growth pattern of children growing normally from birth to adulthood exhibits an "S" shaped pattern with an initial rapid growth that gradually slows down to approach a limit (Hauspie et al., 2004). The distance (upper) and velocity (lower) curves of a female from birth to 18 years are represented graphically in the Figure 1.1 (Hauspie & Roelants, 2013).

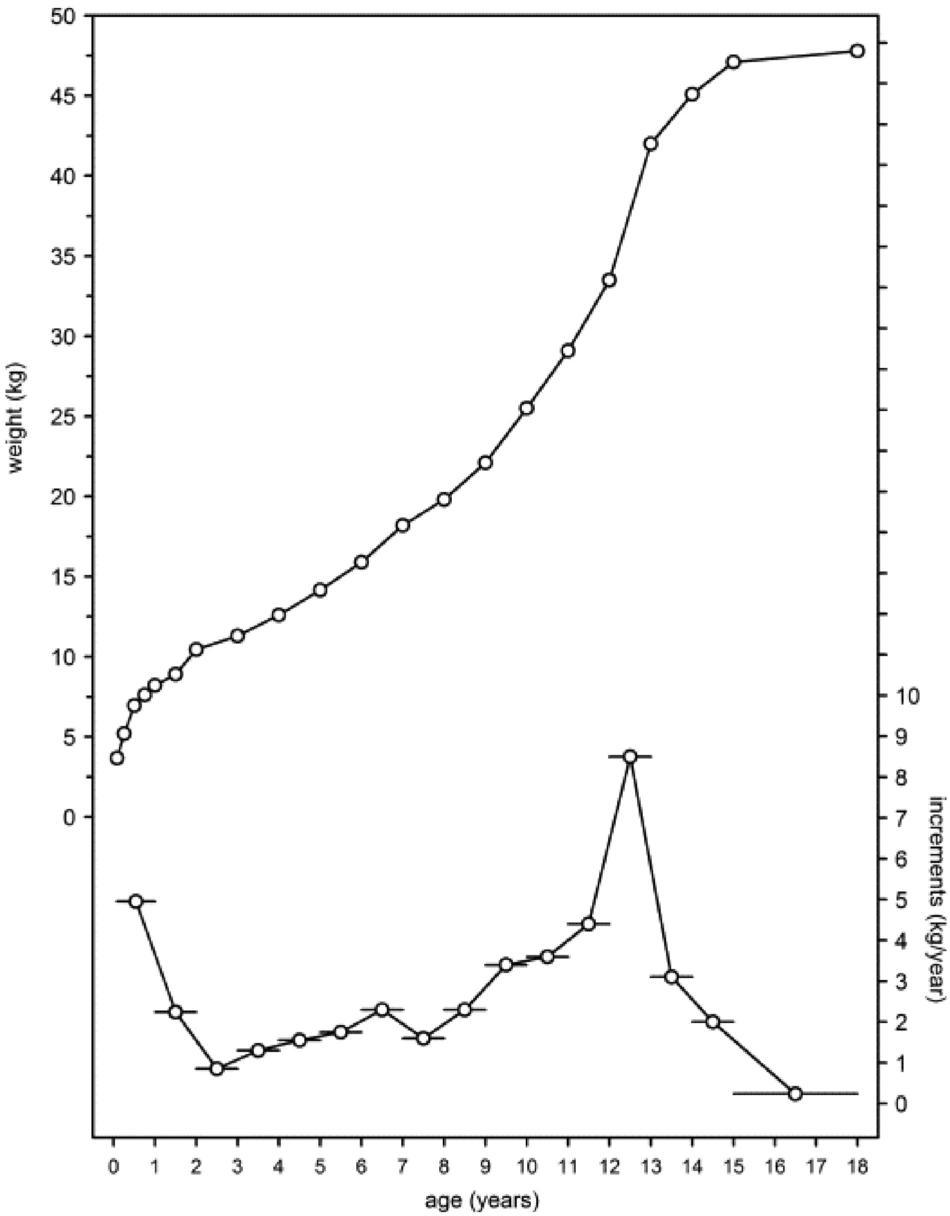

Figure 1.1: Distance and velocity curves of the normal growth of a female from birth to 18 years from source: Hauspie and Roelants (2013)

The growth in weight is somewhat a less regular process than height because the former sometimes experiences greater fluctuations or changes (including decreases) (Silverwood, 2008). Upto 10% of the birth weight is generally lost in the initial days after the child is born. In the first few weeks after the child's birth there is a rapid increase in weight until the age of 1 year with a maximum weight velocity at about 1.5 months (6 weeks). Through a velocity curve, the pattern of growth in weight can be easily described in the postnatal stages (Bogin, 2015). In general, through the velocity curve, the infancy phase shows a gradual or continuous decrease in weight velocity until the age of 3 years (Bogin, 2015). The childhood phase demonstrates a slow decrease in weight velocity alongside more or less a constant rate of growth until the onset of puberty. The adolescence phase is biologically distinctive from the childhood phase. It is associated with the onset of puberty often described as the, "physical transformation of a child into an adult" (Stang & Story, 2005). Puberty is considered a crucial period of the human growth process. During this period, adolescents reach their sexual maturity where they generally experience changes in breasts, genitals, pubic hair, facial hair, deepening of voice and onset of menstruation (Tanner, 1990). They also become capable of sexual reproduction along with the rapid increase in their physical growth appearance (height and weight) (Tanner, 1990). The adolescent or pubertal phase is primarily characterized by an increased or marked acceleration of growth (referred to as an adolescent or pubertal growth spurt) in the adolescents. This growth spurt is then followed by a rapid decrease in weight velocity until the growth ceases and the adolescents reach their final adult body weight (Tanner, 1990; Silverwood, 2008).

The adolescence spurt is a natural phenomenon that occurs in all youth during their course of life although it varies in timing, intensity and duration from one child to another (Tanner, 1981). Timing describes how physically mature the children are in terms of their secondary sexual characteristics when they are compared to the other children of the same sex and age (Marceau, Ram, Houts, Grimm, & Susman, 2011). Depending upon the status of their physical maturity, adolescents are often considered "early", "on time" and "late" maturers (Ge, Brody, Conger, Simons, & Murry, 2002; Hauspie & Roelants, 2013). On the other hand, tempo or intensity are called maturation rate (Tanner, 1962) that describes how quickly children progress along the path to their full sexual maturity (Marceau et al., 2011). It also describes the rate at which the children pass through the late childhood and puberty phase. Depending upon how long it would take them to progress from the prepubertal stage to full maturation, adolescents are considered “slow”, “average” or “fast” maturers (Marceau et al., 2011). The duration of the puberty phase refers to the difference between the ages when it started and ended. Unlike infancy and childhood phases, the interest for the adolescence phase lies in the timing and characteristics of the growth spurt (Beath, 2012). There is a wide variation between populations, between individuals and between the two sexes as to the attained weight at each age, the timing of the adolescent’s growth spurt and the age at which the final weight is reached (Hauspie & Roelants, 2013).

From the research by Tanner and his colleagues (1990), it is known that females’ growth and body structure are quite different from males’. There is a significant difference in their entire growth and development over time. It is indeed specifically during the adolescence years where females start growing earlier and physically faster than males. In general, females’ weigh a little less than males’ at birth (though the difference is quite small) but they catch up and become equal to males approximately at the age 8 (Tanner, 1990). Females’ then become heavier by the age of 9 or 10 years and remains so until the males’ puberty starts. Males’ then again become heavier once the females’ reach the end of their puberty at about 14 or 15 years of age (Tanner, 1990). The normal age for puberty is 8-13 years in girls and 9-14 years in boys (Tanner, 1962). The age at which the weight velocity is maximum is called “age at peak weight velocity”. During the adolescent phase, the difference between the ages of maximum weight velocity in females and males is approximately 2 years. Thus, females’ experience their weight growth spurt earlier than males’ (Tanner, 1962; Bogin, 2015). During puberty, the children gain half of their adult ideal body weight. During puberty, the overall weight gain for females’ is between 7 to 25 kg with a mean gain of 17.5 kg and an average of 8.3 kg per year during peak rates of weight gain (around 12.5 years of age on an average). The gain in weight slows down around the time of menarche in females. For males’, the overall weight gain during adolescence ranges between 7 to 30 kg with a mean gain of 23.7 kg and an average of 9 kg per year (Barnes, 1975; Wong & Wilson, 1995).

Previous studies (Cameron, 2007; Cameron & Bogin, 2012) have defined weight as an eco-sensitive anthropometric measurement that responds more rapidly to any illness and loss of appetite than any other anthropometric measurement. Crucial environmental factors that have major impacts on children's growth include lack of proper nutrition, chronic diseases, poor socioeconomic status, inadequate school and community environments (such as poor access to health care, sanitation services, and recreation activities), psychological stress, depression and lack of physical activity (de Waal, 1993). Cameron (2007) had widely investigated that during childhood and adolescence, those experiencing these environmental factors have important consequences on their weight growth patterns.

Overweight and obesity are defined as unexpected abnormal or rapid gain in weight in infancy and childhood that lead to the long-term deposition of excess abdominal and body fat. Based on the statistics disclosed by the World Health Organisation for the year 2016, the prevalence of overweight and obesity among children and adolescents aged 5-19 years has risen drastically from 4% in 1975 to 18% in 2016 (18% of girls and 19% of boys) (WHO, 2018). Over 340 million children and adolescents aged 5-19 years were overweight and obese in 2016 (WHO, 2018). Being overweight or obese in childhood and adolescence may impair the health condition of an individual that becomes evident in adulthood. Excess body fat in childhood and adolescence is also associated as major risk factors for various chronic diseases in adult life such as cardiovascular disease (coronary artery disease, coronary heart disease), type 2 diabetes (non-insulin dependent), musculoskeletal disorders (osteoarthritis) and cancers (endometrial, breast and colon) (WHO, 2004). Over the past two decades, many studies have largely focused on the rapid weight development in the infancy phase which is associated as a critical factor for adult health (Barker, Osmond, Winter, Margetts, & Simmonds, 1989; Barker, 2004, 2012). Given that adolescence is also the period of the most rapid weight development after infancy, previous studies have demonstrated that it is also a critical and sensitive period for later health and disease (Viner et al., 2015). Pubertal timing (early or later) and the weight gain in puberty may determine the occurrence of a wide range of adverse health problems such as asthma, epilepsy, chronic kidney disease, thyroid dysfunction, diabetes, musculoskeletal pain and mental health problems such as depression, panic attacks, eating disorders and schizophrenia (Patton & Viner, 2007). Excess childhood body fat that later tracks across into adolescence also affects the timing of puberty, and initiates the risk of cardiovascular disease, cancer, obesity and cardiometabolic disease later in adult life (Patton & Viner, 2007).

In order to study various growth patterns, two types of study design are generally used: cross sectional and longitudinal study (Fitzmaurice, Laird, & Ware, 2012). In cross sectional studies, different subjects are measured at different ages. Thus, this study design provides a marginal amount of information about the average growth change or short-term growth trends (Hauspie et al., 2004). On the other hand, for longitudinal studies, the same individuals are measured over many years (Tanner, 1990). These studies can be balanced (individuals have the same number and timing of growth measurements) or unbalanced (number and timing of the measurements can vary between individuals) (Fitzmaurice et al., 2012). Longitudinal studies provide a good description of the growth process as a whole as well as between different growth phases of human life (Hauspie et al., 2004). By employing longitudinal data for the modelling of human growth curves, researchers can easily describe, summarize, visualize, predict and interpret the features of growth patterns (Hauspie et al., 2004).

To thoroughly understand growth trajectories, it is necessary to apply suitable mathematical models to longitudinal growth data. The findings from the fitted growth models will aid to determine the individuals those at risk for future disease and its associated complications in adult life with the aim of taking precautions and preventions beforehand.

1.2 Literature review

1.2.1 Child growth models

The child growth curve models refer to a broad spectrum of statistical models for modelling children's longitudinal data. They are often defined as the mathematical representations of the human growth process. These mathematical representations summarize the huge amount of sample growth data into meaningful growth patterns and estimation of limited number of growth parameters. These estimated parameter values are further used to make valid inferences about the population from which the sample has been drawn (Hauspie et al., 2004). According to the paper by Berkey (1982), a growth model is considered to be ideal when it: has a simple fitting procedure, provides a satisfactory fit to the data, has biological interpretations of the parameters, and provides decent prediction.

A number of mathematical growth models have been introduced in the literature. Generally, the growth models are classified into two types: parametric (structural) and non-parametric (non-structural) models (Hauspie et al., 2004). Polynomials and splines (Largo, Gasser, Prader, Stuetzle, & Huber, 1978; Pan & Goldstein, 1998) are the most common examples of non-parametric models. These non-parametric models are very general and can be used to fit growth data in any anthropometric variable over any age range (Silverwood, 2008). Hauspie and his colleagues (Hauspie et al., 2004) summarized various differences between parametric and non-parametric models. Non-parametric models are easy to fit. But these models come with a limitation that they contain a large number of coefficients that need to be estimated and the parameters do not have any biological interpretations. These models provide good or almost accurate approximations to the values within the observed data but generally have a poor fit at the tails of the sample data. Also, these models do not provide reliable predictions of the outcome outside the observed range of data. The estimated growth curves from the non-parametric models do not take any specific shape. Rather, these curves usually take the shape of the data. They are inefficient to fit a larger age range, and do not reach an upper asymptotic value at the end of the adolescent growth phase. Compared to non-structural models, the structural models have less parameters to estimate (Hauspie et al., 2004). These structural models exhibit basic functional form of the growth model and tend to reach an upper asymptote (Hauspie et al., 2004).

In previous studies, researchers have recommended and developed many parametric models for children's growth. In comparison to the non-parametric models, the parametric models were proposed mainly because of their ability to provide a good fit to the growth data with a minimum number of parameters (Beath, 2012). In the literature, parametric models that were most often applied were developed by Jenss-Bayley (1937), Count (1943) and Berkey and Reed (1987).

The Jenss-Bayley model (Jenss & Bayley, 1937) is a combination of linear and non-linear (exponential) components. This model satisfactorily describes infant and childhood growth data during the first 6 years of life (Jenss & Bayley, 1937). Historically, the Jenss-Bayley curve was successfully used to model length and weight during the first 8 years of life in healthy American boys and girls (Deming & Washburn, 1963). Later, the model was applied to model growth pattern of height, weight and skull circumference in the first year of life in a sample of Indian children (Manwani & Agarwal, 1973). The Jenss-Bayley model was also used in various other studies (Berkey, 1982; Dwyer, Andrew, Berkey, Valadian, & Reed, 1983; Karlberg, 1990).

Several years after the original Jenss-Bayley model, Count (1943) proposed another major growth function called the Count model. The latter model was originally used to model height. The model was later applied to describe both height and weight growth patterns from birth to 6 years (Berkey, 1982). In order to model the data from birth, the Count model was slightly modified by shifting the age scale. It is a linear model that includes a logarithmic term.

In the literature, comparisons were conducted between various parametric growth models. Berkey (1982) compared Jenss-Bayley (1937) and Count (1943) models for both height and weight in a longitudinal sample of healthy Boston children from 3 months to 6 years of age. The author concluded that the Jenss-Bayley model not only generally provided the better fit to height and weight at every age, but it outperformed the Count model based on reliability, precision, and efficiency. The Count model overall did not perform well and also showed systematic deficiencies at each age. The results were consistent with a previous investigation fitting three linear growth models from birth to 2 years of age, each one of them having three parameters to be estimated (Wingerd, 1970). Thus, from this study, the researchers concluded that a linear model with at least four parameters were required to model early childhood growth data (Berkey, 1982).

In order to overcome the age-related deficiencies of the Count model, Berkey and Reed (1987) increased the flexibility of the model by adding an extra term in order to improve the fit of the model. Hence, Reed 1^{st} order model (Berkey & Reed, 1987) is an extension of the Count model (Count, 1943). Like the Jenss-Bayley model, this model also explains early childhood growth from birth to 6 years. To further describe abnormal growth patterns among children, another term was added to Reed 1^{st} order to obtain Reed 2^{nd} order model (Berkey & Reed, 1987). These models (Jenss-Bayley, Count and Reed 1^{st} order models) were compared by Berkey and Reed (1987) where the newly developed Reed 1^{st} order model was found to be a significantly better fit than the others.

The Reed 1^{st} and 2^{nd} order models have been considered superior than other previously developed growth models because they can accommodate a variety of normal and abnormal growth patterns during early life growth (Berkey & Reed, 1987). Lastly, an Adapted Jenss-Bayley model has been proposed in the literature in order to extend the age range from birth to puberty (Botton et al., 2008).

However, the major drawback of these various parametric models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, Adapted Jenss-Bayley) is that the estimated parameters of these models do not have any biological interpretations (Jenss & Bayley, 1937; Berkey & Reed, 1987; Botton et al., 2008). Traditionally, these models were applied to model each child separately in order to obtain an individual's growth curve (Tanner, 1990). To overcome the latter problem, researchers have suggested an alternative approach for modelling longitudinal data called mixed models (also known as random effect, multilevel or hierarchical models) (Pinheiro & Bates, 2000; Fitzmaurice et al., 2012). This approach consists of fitting any selected model using fixed effects and random effects of the model parameters. Thus, this technique models all the children simultaneously rather than fitting them individually. In general, the purpose for using mixed models is that that they can estimate inter-individual variability in intra-individual patterns of growth change over time (Curran, Obeidat, & Losardo, 2010; Fitzmaurice et al., 2012). Traditionally, the fixed effects models do not make any assumptions about the distribution of the parameters. In contrast, the mixed models assume that the parameters of Jenss-Bayley, Reed 1^{st} order, 2^{nd} order and Adapted Jenss-Bayley models are drawn from a multivariate normal distribution with mean 0 and variance covariance matrix ϕ and are independent of the errors which are normally distributed with mean 0 and constant variance σ^2.

Within a mixed model framework, application of the previous models in the literature includes utilizing the Jenss-Bayley model to describe the height trajectories of children to detect individuals with Turner syndrome (van Dommelen, van Buuren, Zandwijken, & Verkerk, 2005). For the Reed model, a mixed model approach was used to analyze growth in weight during the early years of life in an Ethiopian (birth to 1 year) and a Finnish birth cohort (birth to 2 years) (Asefa, Drewett, & Hewison, 1996; Tzoulaki et al., 2010).

Several studies have been conducted to compare these anthropometric models using a mixed model approach. Researchers compared several growth models (Reed 1^{st} order, Reed 2^{nd} order, Count were amongsters) for modelling weight among 95 rural Congolese infants between birth and 13 months of age (Simondon, Simondon, Delpeuch, & Cornu, 1992). The authors found that the Reed 1^{st} order model fitted the best in comparison to the other models. In a recent paper, Chirwa et al. (2014) compared structural (Reed 1^{st} order, Count, Jenss-Bayley and the Adapted Jenss-Bayley) and non-structural models (2^{nd} and 3^{rd} order Polynomials) to model weight and height from birth to ten years of age in a longitudinal urban South African study. It was found that the Reed 1^{st} order model was the best fitted growth model as compared to others for weight and height from birth to pre-puberty. In contrast, a comparison of four growth models (Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} order and Reed 2^{nd} order) for weight and height by N. Regnault et al. (2014) in US children from birth to 9 years showed that Adapted Jenss-Bayley model fitted the best.

Thus, the mixed model approach is very flexible for modelling longitudinal data as it allows to model all the subjects simultaneously. However, these growth models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order and Adapted Jenss-Bayley) continue to share one key limitation: the derived parameters have no biological interpretation. This limitation was addressed by a new model proposed by Cole et al. (2010) called SITAR (SuperImposition by Translation And Rotation)– a semi parametric non-linear random effect model (Cole, Donaldson, & Ben-Shlomo, 2010; Pizzi et al., 2014).

The SITAR model is an extension of shape invariant growth modeling, an improved technique which was proposed by Beath (2007) to model weight in infants. The authors (Lawton, Sylvestre, & Maggio, 1972) originally introduced the Shape invariant model concept but it was applied later to model human growth (Stützle et al., 1980). In the SITAR model, a natural cubic spline function is fitted that estimates the average growth curve which is common for all the individuals in the sample. Apart from the cubic spline function, the model also includes three parameters that adjusts the common average growth curve to fit to each individual growth trajectory. All parameters have biological interpretations (Beath, 2007; Cole et al., 2010). Cole et al. (2010) further used the SITAR model to model height from onset of puberty to adulthood (9 to 19 years of age) (Hui, Leung, Cowling, Lam, & Schooling, 2010; Johnson, Llewellyn, Jaarsveld, Cole, & Wardle, 2011).

Later Pizzi et al. (2014) compared Jenss-Bayley, Reed 1^{st} order model within the mixed effect framework, and the recently developed SITAR model in order to describe weight in children from birth to 4 years of age in three different cohorts for females and males separately. Based on Akaike information criterion (AIC) and Bayesian information criterion (BIC) fit statistics, the Reed 1^{st} order model performed better than the other two models in both sexes, but the SITAR model was found to be a better fit than the Jenss-Bayley model. The SITAR model was shown to be superior than Jenss-Bayley and Reed 1^{st} order models because it identified the peak in the growth curve where other models failed to identify. Moreover, the SITAR model estimated parameters were biologically interpretable (Pizzi et al., 2014). A recent study showed that by pooling NSHD (National Survey of Health and Development) and ALSPAC (Avon Longitudinal Study of Parents and Children) data, the SITAR model was successful in demonstrating that the pubertal timing in height and weight has an effect on the bone health (skeletal and osteoporosis risk) in early old age (Cole et al., 2016). In a recent study, the authors used SITAR model to classify pregnancy or gestational weight gain growth patterns in women (Riddell, Platt, Bodnar, & Hutcheon, 2017). The SITAR model was also applied in the age group 1 to 20 years to identify secular trend patterns in height and weight growth in Japan and South Korea over 50 years (Cole & Mori, 2018).

To date, the most commonly used parametric models (Jenss-Bayley, Reed 1^{st} and 2^{nd} order) have been applied to a small age range of children (from birth until middle or late childhood) for height and weight. The Adapted Jenss-Bayley model has been applied to model child's growth from birth to puberty. None of these parametric models possess any biological interpretation of their coefficients. The recently developed SITAR model has been applied to various age ranges and has biological interpretation of its parameters. However, a comparison of these models in fitting childhood and adolescent data has never been conducted. Thus, this study focuses on modelling weight change in children from their middle childhood age to adolescence phase. More specifically, this study aims to extend and compare these models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, Adapted Jenss-Bayley, and SITAR) within the mixed effect framework to model longitudinal weight in an age range of children that starts from middle childhood and includes puberty (6 to 15 years).

Chapter 2

Subjects and Methods

2.1 Data description

Data for this study are obtained from the Quebec Longitudinal Study of Child Development (QLSCD), a birth cohort that was initiated by Direction Santé Québec (Health Quebec Division) in collaboration with various Quebec universities (Jetté & Groseillers, 2000). The main purpose of the original longitudinal study was to assess the determinants that could affect the development, psycho-social adaptations, and academic success of a representative sample of Québec children (Jetté & Groseillers, 2000). Data collection is going.

The targeted population was singleton births born in the province of Quebec, Canada. Children were recruited from a Master Quebec live birth registry of the ministère de la Santé et des Services sociaux (MSSS) of the 1997-1998 year. Exclusion criteria included children without gender specification indicated in the hospital record, unspecified mother's pregnancy duration in the birth record, born before 24 weeks (premature) or after 42 weeks, born in Northern region of Quebec, Cree and Inuit territories or on Indian reserves where aboriginal people live. Through a stratified multi-stage sampling design, an initial sample (n = 2,940) of singleton live births were selected as representative of the target population after these exclusions. Further, n = 265 were excluded from the initial sample because the families of the children were living permanently outside the Quebec province, were unreachable (incorrect addresses and telephone numbers), were not responding after several attempts, or neither speak nor understand English or French. Families of n = 2,675 were reachable but $n = 452$ were additionally excluded if the child was born with serious health conditions (such as physically or mentally handicapped), had died, or the family was currently participating in any other longitudinal study. Thus, after these exclusions $n = 2{,}223$ were the respondents selected from the initial sample. Children ($n = 103$) who were initially included to determine the effect of a natural disaster (January 1998 ice storm) were subsequently removed. Thus, a total of ($n = 2{,}120$) children were selected for the QLSCD birth cohort (Jetté & Groseillers, 2000; Jetté, 2002).

To date, three phases have been completed by this ongoing study:- phase 1 (1998-2002) aimed for children from 5 months to 4 years, phase 2 (2003-2010) from 5 years to 12 years, phase 3 (2011-2015) from 13 to 17 years and phase 4 (started in 2016 and to be completed by 2023) from 19 to 25 years (Detailed information of the phases are available at the website `http://www.iamillbe.stat.gouv.qc.ca/default_an.htm`). The children were followed approximately annually (from birth to 8 years) and then bi-annually (from age 8 and on). The study was approved by the Ethics Committee of the Santé Québec Division (le Comité d'éthique de la Direction Santé Québec) (Jetté & Groseillers, 2000; Jetté, 2002).

Several data collection tools were applied to collect information about the children and their respective families. These tools included computerized questionnaires and paper questionnaires administered to the parent(s), teachers, and the child (once the children reached the age 6+). However, because weight was the main variable of interest to this study, other than demographic information, the child-reported, parent-reported, and teacher-reported data were not used for this study (More details on the data collection tools used in the study are available from the website `http://www.iamillbe.stat.gouv.qc.ca/default_an.htm`). Parent(s) of the participants signed the consent form annually, and were later signed by teachers and participants, when the children started going to school (Jetté & Groseillers, 2000).

The data available for this research study are from birth to 15 years of age. In the QLSCD study, the child's weight was measured at birth and further weight measurements were collected at approximately 5, 17, 29 and 41 months, and then at 5, 6, 7, 8, 10, 12, 13 and 15 years of age. As the child's weight measurements under 6 years of age were self-reported by the parents (Jetté & Groseillers, 2000) and were subject to bias (Mathieu, Drapeau, & Tremblay, 2010), only the objective measures of weight were used for this study. Thus, the present research employs weight measurements when the children were 6 to 15 years of age. For these data collection waves of interest, the participant's body weight was measured in duplicate using a spring balance by a trained staff member, recorded in kilograms and set again to zero for each measurement (http://www.iamillbe.stat.gouv.qc.ca/default_an.htm). The children were dressed lightly and without shoes. If the difference between the first two measurements was 0.2 kg or more, a third measurement was collected. The average value of the closest two measurements was calculated and were used as the participant's body weight for this research analysis.

2.2 Methods

An overview of all growth models of interest for this study is below. Each growth model's original as well as mixed effects specifications is provided.

2.2.1 Jenss-Bayley model

2.2.1.1 Original specification

The Jenss-Bayley model (Jenss & Bayley, 1937) is a monotonic non-linear longitudinal model consisting of four parameters with a negatively accelerated exponential curve in t that approaches a linear asymptote (a straight line with a positive slope). Researchers have widely applied this model to describe growth patterns of children's height, weight and head circumference for the period from birth to 8 years (Jenss & Bayley, 1937; Deming & Washburn, 1963; Manwani & Agarwal, 1973; van Dommelen et al., 2005). This model captures initial rapid growth after birth, a continuous decrease in growth rate in infancy phase followed by the linear pattern during early childhood to middle childhood. The Jenss-Bayley model can be fitted using non-linear regression.

To model weight using the Jenss-Bayley model, the age of the subjects could be defined in days/weeks/months/years. For the purpose of this study, age is defined in months. For the ease of interpretation, all the Figures in this study represents the age in years. According to Jenss-Bayley (1937), the original model was defined as $y_i(t) = c_i + d_i t - e^{(a_i + b_i t)} + \epsilon_{it}$ for i = 1, 2.... N and t = 1, 2.... T_i. In order to be consistent with the other growth models and for the ease of interpretation, the notations c_i, d_i, a_i

and d_i are defined as a_i, b_i, c_i and d_i in this study and the redefined model is represented below in equation (1).

The Jenss-Bayley model specification pertinent to this research in weight change for subjects from 6 to 15 years of age is as follows:

For subjects $i = 1, 2 \ldots\ldots N$ and time points $t = 1, 2 \ldots\ldots T_i$

$$y_i(t) = a_i + b_i t - e^{(c_i + d_i t)} + \epsilon_{it} \quad (1)$$

where

$y_i(t)$ = weight measured for individual i at age t (kg)

t = age (time) variable (years)

a_i = individual's intercept of the asymptote of the distance curve (kg)

b_i = individual's basic rate of growth (kg per year)

e^{c_i} = the vertical distance between the intercept of the distance curve and intercept of its asymptote for each individual (kg)

e^{d_i} = each individual's acceleration growth constant

$e^{(c_i+d_i t)}$ = at any point on the distance curve, the vertical distance between the curve and its asymptote for each individual (decelerating rate of growth)

When the birth data is included the predicted/estimated weight (kg) at birth for ith individual is defined as a_i - e^{c_i}. In general, this model consists of a linear part (a_i + $b_i t$) and a non-linear part $e^{(c_i+d_i t)}$ where a_i, b_i, c_i and d_i are the unknown parameters to be estimated for each child separately. ϵ_{it} is the measurement error term at age t specific to child i, that is assumed to be normally distributed with mean 0 and constant variance σ_i^2 (van Dommelen et al., 2005; Pizzi et al., 2014). According to Jenss-Bayley (1937), the model takes into account rapid decelerating rate of growth generally observed after birth through an exponential component $e^{(c_i+d_i t)}$ where e^{d_i} is defined as the ratio of growth acceleration at any time point, to the acceleration one time point previously for each individual. This acceleration growth constant is a pure number, non-dimensional, and independent of the unit of time measurement that is used. The exponential component $e^{(c_i+d_i t)}$ does not contribute much after the infancy phase as the growth becomes steady and linear (Berkey & Reed, 1987). The shape of the individual's growth curve is usually determined by this growth constant (Deming & Washburn, 1963). A small acceleration growth constant provides more curvature at the early ages and an early approach to the asymptote. On the other hand, large values provide a flat curve and a later approach to its asymptote (Deming & Washburn, 1963).

The parameters of the Jenss-Bayley model are graphically described by Deming and Washburn (1963) and can be seen below in Figure 2.1. The graph depicts that the growth curve is fitted using the Jenss-Bayley model to describe longitudinal length measurements for one girl from birth to 8 years of age. The estimated Jenss-Bayley curve for the girl is $y = a + bx$ - $e^{(c+dx)}$ where $x =$ time in months, $a = 82.5$ cm (intercept of the asymptote), $b = 0.575$ cm per month (slope of the asymptote), $e^c = 29.579$ (intercept of the curve), $e^d = 0.934$ (acceleration growth constant) where $d =$ -0.0682 and a - $e^c = 52.925$ cm (height at birth) (Deming & Washburn, 1963).

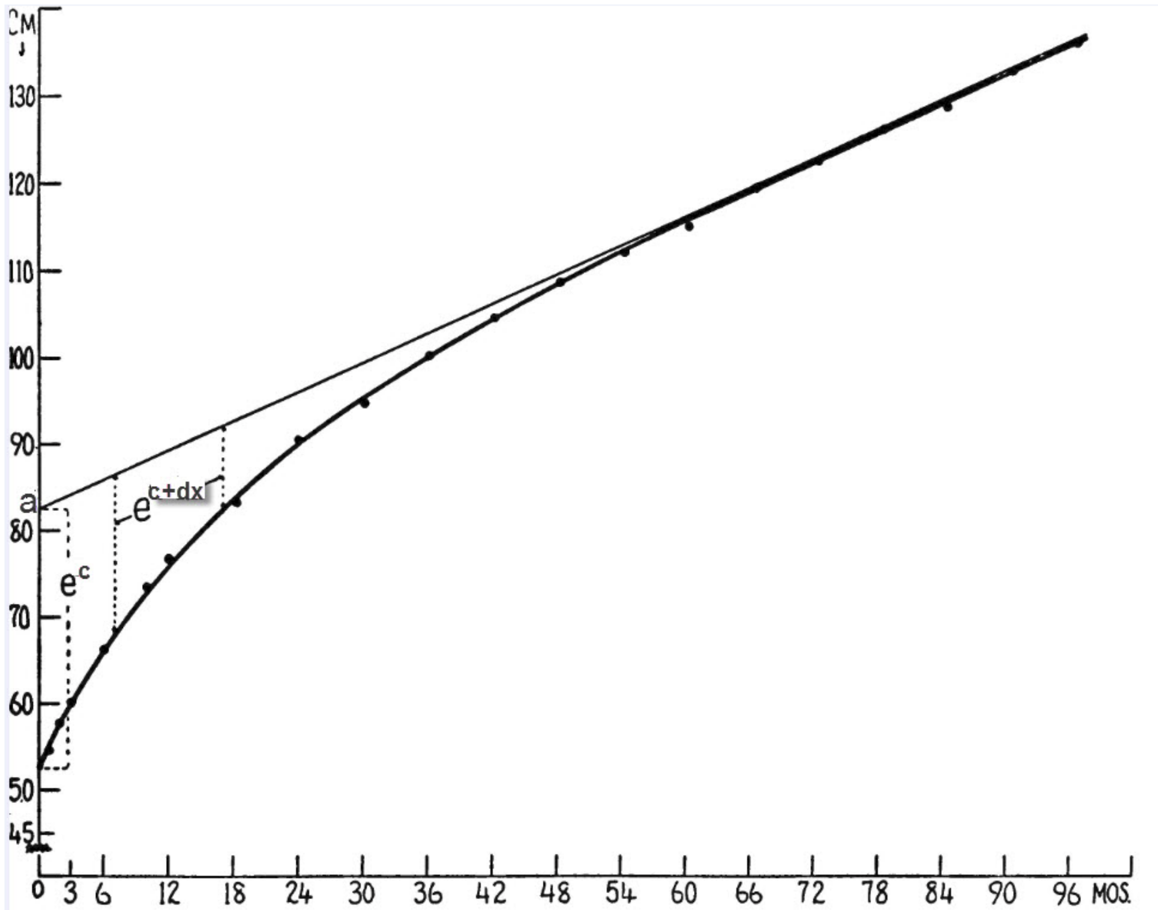

Figure 2.1: Graphical description of the Jenss-Bayley model parameters adapted from source: Deming and Washburn (1963)

The absolute rate of velocity curve at any point on the curve is obtained by differentiating the Jenss-Bayley function with respect to t and is expressed as $dy/dt = b - de^{(c+dt)}$ whereas the acceleration curve is obtained by differentiating the velocity curve with respect to t or second differentiation of the distance curve and is expressed as $d^2y/dt^2 = -d^2e^{(c+dt)}$. As time t increases, the acceleration growth constant e^{dt} increases, thus the deceleration term $e^{(c+dt)}$ decreases leading to an increase in the magnitude of y though not uniformly but approaching to the asymptote $(a + bt)$. At the same time, the velocity approaches to the basic growth rate b alongside a progressive decrease in the magnitude of the negative acceleration approaching to zero (Deming & Washburn, 1963).

2.2.1.2 Mixed effects specification

The original specification of the Jenss-Bayley models each individual separately and does not possess any distributional assumptions of its parameters. Thus, Pizzi et al. (2014) recommended to extend this model by integrating random effects. To define a growth function that models all children simultaneously, some distributional assumptions for the child-specific parameters and their relation with the residual errors ϵ_{it} are needed. To estimate the parameters of the Jenss-Bayley model, a mixed effects model approach is used. In mixed effect model specification, the model assumes that each growth parameter in the model is the sum of a fixed effect component and a random effect component. The fixed effect is the same for all the individuals representing an average value and the random effect is allowed to vary over each individual (van Dommelen et al., 2005) representing standard deviation around the average value. The mixed effect specification representing the growth at time t indicates the average population growth that is shared by all the individuals and child-specific or random effects that describes how each subject's growth deviates from the average population growth. Using the same notation as in equation (1), the parameters a_i, b_i, c_i and d_i are defined as:

$a_i = a_0 + a_{1i}$

$b_i = b_0 + b_{1i}$

$c_i = c_0 + c_{1i}$

$d_i = d_0 + d_{1i}$

where a_0, b_0, c_0 and d_0 represents the fixed effects and a_{1i}, b_{1i}, c_{1i} and d_{1i} represents the random effects of the growth parameters a_i, b_i, c_i and d_i respectively. These extensions assume that the child-specific random effects a_{1i}, b_{1i}, c_{1i} and d_{1i} are drawn from a multivariate normal distribution with mean 0 and variance-covariance matrix ϕ and are independent for different subjects (Pinheiro & Bates, 2000). The errors ϵ_{it} are independent and identically normally distributed random variables with mean 0 and constant variance σ^2, which are independent of the child-specific random effects. When the random effects in the growth model are equated to zero, the curve implied by the model $a_0 + b_0$t - $e^{(c_0+d_0t)}$ is called a population level curve (Pinheiro & Bates, 2000).

2.2.2 Reed 1^{st} order model

2.2.2.1 Original specification

Berkey and Reed (1987) introduced another growth function called the Reed model, a linear model appropriate for modelling early childhood growth in length, weight and head circumference for normally growing children. Both Jenss-Bayley and Reed 1^{st} order models have four parameters. Unlike the Jenss-Bayley model, the Reed model is linear in its parameters and can be fitted by linear regression. As compared to non-linear growth models, analysis of parameters and fitting of the curve is simpler.

The specification of the Reed 1^{st} order model pertinent to this research is as follows:

For subjects $i = 1, 2.....N$ and time points t = 1, 2.....T_i

$$y_i^{'}(t) = a_i^{'} + b_i^{'}t + c_i^{'}ln(t) + d_i^{'}(1/t) + \epsilon_{it}^{'} \tag{2}$$

where

$y_i^{'}(t)$ = weight measured for child i at age t (kg)

t = age (time) variable (years)

$a_i^{'}$ = child's intercept of the asymptote of the distance curve (kg)

$b_i^{'}$ = child's slope of the asymptote (kg per year)

$c_i^{'}$, $d_i^{'}$ = decreasing growth velocity for each subject (deceleration parameters)

The Reed model (Berkey & Reed, 1987) is an extension of the Count model (Count, 1943) which is expressed as $y_i^{'}(t) = a_i^{'} + b_i^{'}t + c_i^{'}ln(t) + \epsilon_{it}^{'}$. The parameters $a_i^{'}$, $b_i^{'}$ and $c_i^{'}$ for the Count model have the same interpretation as above. In contrast to the Count model, the Reed 1^{st} order model incorporated another deceleration term $d_i^{'}(1/t)$ to improve the fit of the model (Beath, 2012). The additional deceleration term $d_i^{'}(1/t)$ in the Reed model behaves very similarly to the exponential component of the Jenss-Bayley model (Jenss & Bayley, 1937) by capturing the decreasing growth velocity during infancy. The velocity curves of the Reed model ($b^{'}$ + $c^{'}/t$ - $d^{'}/t^2$) and Count model ($b^{'}$ + $c^{'}/t$) are polynomial functions of ($1/t$) (reciprocal of age), thus they are also called reciprocal models (Berkey & Reed, 1987). Both Jenss-Bayley and Reed models are equally prepared to handle the data that doesn't necessarily start at birth. But if birth data is included, then the chronological age since birth cannot be considered in the Reed model because the natural logarithm of age (logarithm of 0 ($ln(0)$)) and inverse of age (1/0) are not defined and hence an alternative age scale is required. To account for this, the Reed model suggested an age transformation as $t^* = (t+9)/9$ where t = age in months since birth assigning $t^* = 0$ at conception and $t^* = 1$ at birth. In theory, an alternative transformation was also proposed by adding a value of 1 to the time variable only where the logarithmic and inverse functions are of time. Using this transformation (Count, 1943), the age transformed Reed 1^{st} order model (equation (2)) can be expressed as:

$y_i^{'}(t) = a_i^{'} + b_i^{'}t + c_i^{'}ln(t+1) + d_i^{'}(1/t+1) + \epsilon_{it}^{'}$ for subjects $i = 1, 2\ldots\ldots N$ and time points $t = 1, 2\ldots\ldots T_i$

This transformation describes ($a^{'} + b^{'} + d^{'}$) weight at birth and ($b^{'} + c^{'}$ - $d^{'}$) velocity at birth that approaches to b, preschool period velocity. The $a_i^{'}$, $b_i^{'}$, $c_i^{'}$ and $d_i^{'}$ are unknown growth parameters to be estimated for each child separately and $\epsilon_{it}^{'}$ is the error term specific to child i at age t, that is assumed to be normally distributed with mean 0 and variance $\sigma_i^{'2}$.

2.2.2.2 Mixed effects specification

Using mixed effect modelling approach, the parameters of the Reed 1^{st} order model (equation (2)) are defined as:

$a_i^{'} = a_0^{'} + a_{1i}^{'}$
$b_i^{'} = b_0^{'} + b_{1i}^{'}$
$c_i^{'} = c_0^{'} + c_{1i}^{'}$
$d_i^{'} = d_0^{'} + d_{1i}^{'}$

where the fixed effects are represented by $a_0^{'}$, $b_0^{'}$, $c_0^{'}$ and $d_0^{'}$ and $a_{1i}^{'}$, $b_{1i}^{'}$, $c_{1i}^{'}$ and $d_{1i}^{'}$ are represented by child-specific random effects of the growth parameters $a_i^{'}$, $b_i^{'}$, $c_i^{'}$ and $d_i^{'}$ respectively. The parameters $a_{1i}^{'}$, $b_{1i}^{'}$, $c_{1i}^{'}$ and $d_{1i}^{'}$ are child-specific random effects assumed to be drawn from a multivariate normal distribution with mean 0 and covariance matrix $\phi^{'}$. The errors $\epsilon_{it}^{'}$ are independent and identically normally distributed random variables (mean 0 and constant variance σ'^2) and are independent of the child-specific random effects. Unlike the Jenss-Bayley model, this model can accommodate one inflection point in the curve and hence Age at Peak Weight Velocity (APWV) can be obtained by differentiating the weight velocity curve dy/dt and then equating it to zero (i.e. $d^2y/dt^2 = 0$).

2.2.3 Reed 2^{nd} order model

2.2.3.1 Original specification

Reed 2^{nd} order is an extension of the Reed 1^{st} order model developed by Berkey and Reed (1987). This model is a linear model with five parameters and can be easily fitted with linear least square regression. Reed 2^{nd} order is obtained by adding another deceleration term to the Reed 1^{st} order model to provide a significant improvement over the four-parameter Reed model. This model is useful to describe unusual or abnormal growth patterns among children that cannot be modelled well by the Reed 1^{st} order model. It is sometimes referred to as the five parameter Reed model.

The Reed 2^{nd} order model specification for this research study for subjects $i = 1, 2 \ldots N$ and time points $t = 1,\ 2 \ldots T_i$ is as follows:

$$y_i''(t) = a_i'' + b_i''t + c_i''ln(t) + d_i''(1/t) + e_i''(1/t^2) + \epsilon_{it}'' \tag{3}$$

where

$y_i''(t)$ = weight measured for child i at age t (kg)

t = age (time) (years)

a_i'' = child's intercept of the asymptote (kg)

b_i'' = child's slope of the asymptote (kg per year)

c_i'', d_i'', e_i'' = decreasing growth velocity for each subject (deceleration parameters)

Estimation of the unknown growth parameters in the model is done separately for each child. The error term ϵ_{it}'' is specific to each child at age t and assumed to be normally distributed with mean 0 and variance $\sigma_i''^2$.

Using the age transformation suggested by Berkey and Reed (1987) mentioned above, the Reed 2^{nd}

order model (equation (3)) for subjects $i = 1, 2. \ldots\ldots N$ and time points $t = 1,\ 2. \ldots\ldots T_i$ is defined as:

$$y_i^{''} = a_i^{''} + b_i^{''} + c_i^{''} ln(t+1) + d_i^{''}(1/(t+1)) + e_i^{''}(1/t^2) + \epsilon_{it}^{''}$$

In general, Reed models with order greater than one can handle more than one period of growth acceleration indicated by the presence of more than one inflection point.

2.2.3.2 Mixed effects specification

Specifying Reed 2^{nd} order model (equation (3)) within the mixed effect framework, the growth parameters are defined as

$$a_i^{''} = a_0^{''} + a_{1i}^{''}$$
$$b_i^{''} = b_0^{''} + b_{1i}^{''}$$
$$c_i^{''} = c_0^{''} + c_{1i}^{''}$$
$$d_i^{''} = d_0^{''} + d_{1i}^{''}$$
$$e_i^{''} = e_0^{''} + e_{1i}^{''}$$

where $a_0^{''}$, $b_0^{''}$, $c_0^{''}$, $d_0^{''}$, $e_0^{''}$ represents the fixed effects and $a_{1i}^{''}$, $b_{1i}^{''}$, $c_{1i}^{''}$, $d_{1i}^{''}$, $e_{1i}^{''}$ represents random effects. The parameters $a_i^{''}$, $b_i^{''}$, $c_i^{''}$, $d_i^{''}$ and $e_i^{''}$ are assumed to be drawn from a multivariate normal distribution with mean 0 and variance-covariance matrix $\phi^{''}$ and that the errors $\epsilon_{it}^{''}$ are independent, normally distributed random variable with mean 0 and constant variance $\sigma^{''2}$, which are independent of the child-specific random effects. This model can accommodate at most two inflection points in the growth curve.

2.2.4 Adapted Jenss-Bayley model

2.2.4.1 Original specification

An extension of the original Jenss-Bayley model (Jenss & Bayley, 1937) was proposed by Botton et al. (2008) known as the Adapted Jenss-Bayley model. This model has the same four parameters as in the initial Jenss-Bayley model plus an additional quadratic term in age. This five-parameter non-linear Adapted Jenss-Bayley model enables modelling child's growth (weight and height) from birth to puberty instead of from birth to eight years of age as defined in the original Jenss-Bayley model. This model consists of two components: a linear component $a_i^{'''} + b_i^{'''}t + e_i^{'''}t^2$ that models growth (primarily after 3 years of age), plus an exponential component $e^{(c_i^{'''} + d_i^{'''}t)}$ that models decreasing growth velocity shortly after birth during the child's first three years (van Dommelen et al., 2005; Botton et al., 2008).

The Adapted Jenss-Bayley model specification for this research study for subjects $i = 1, 2...N$ and time points t = 1, 2...T_i is expressed as:

$$y_i^{'''}(t) = a_i^{'''} + b_i^{'''}t \text{ - } e^{(c_i^{'''} + d_i^{'''}t)} + e_i^{'''}t^2 + \epsilon_{it}^{'''} \quad (4)$$

where

$y_i^{'''}(t)$ = weight measured for child i at age t (kg)
t = age (time) variable (years)
$a_i^{'''}$ = intercept of each child's asymptote at time of the distance curve (kg)
$b_i^{'''}$ = slope of each child's asymptote (constant rate of growth) (kg per year)
$e^{c_i^{'''}}$ = the vertical distance between the intercept of the growth curve and intercept of the asymptote for each child (kg)
$e^{d_i^{'''}}$ = each child's acceleration growth constant
$e^{(c_i^{'''} + d_i^{'''}t)}$ = at any point on the distance curve, the vertical distance between the distance curve and its asymptote for each individual (decelerating rate of growth).
$e_i^{'''}$ = captures child's growth velocity at the onset of puberty (kg per year)

The unknown growth parameters $a_i^{'''}$, $b_i^{'''}$, $c_i^{'''}$ and $d_i^{'''}$ are to be estimated separately for each child. The $\epsilon_{it}^{'''}$ is the error term specific for each child i at age t and assumed to follow normal distribution with mean 0 and variance $\sigma^{'''2}$. $a_i^{'''}$ - $e^{c_i^{'''}}$ is the predicted weight (kg) at birth for child i when the birth data is included.

2.2.4.2 Mixed effects specification

The parameters of the Adapted Jenss-Bayley model (equation (4)) in a mixed effect model are expressed as:

$a_i^{'''} = a_0^{'''} + a_{1i}^{'''}$
$b_i^{'''} = b_0^{'''} + b_{1i}^{'''}$
$c_i^{'''} = c_0^{'''} + c_{1i}^{'''}$
$d_i^{'''} = d_0^{'''} + d_{1i}^{'''}$
$e_i^{'''} = e_0^{'''} + e_{1i}^{'''}$

where $a_0^{'''}$, $b_0^{'''}$, $c_0^{'''}$, $d_0^{'''}$ and $e_0^{'''}$ are the fixed effects and $a_{1i}^{'''}$, $b_{1i}^{'''}$, $c_{1i}^{'''}$, $d_{1i}^{'''}$ and $e_{1i}^{'''}$ are the random effects respectively. The parameters $a_{1i}^{'''}$, $b_{1i}^{'''}$, $c_{1i}^{'''}$, $d_{1i}^{'''}$ and $e_{1i}^{'''}$ are assumed to be drawn from a multivariate normal distribution with mean 0 and covariance matrix $\phi^{'''}$. The errors are independent, normally distributed random variable with mean 0 and constant variance $\sigma^{'''2}$ which are independent of the child-specific random effects.

2.2.5 SITAR model

A growth model was introduced by Beath (2007) known as the Shape invariant model (SIM) to describe weight data in infants from birth to two years. The important feature of this model as compared to other previously mentioned parametric growth models is that its parameters have direct biological interpretations of the human growth process. Later Cole et al. (2010) extended the shape invariant model and named it as SuperImposition by Translation And Rotation (SITAR). This model estimates the sample average growth curve using natural cubic spline function. The spline function in the model captures non-linearity in the data and also identifies inflection points. Moreover, this average curve can be used to fit each individual's growth curve by shifting the x and y axes and scaling the x-axis. The model was fitted by using a non-linear mixed effects approach. The common spline function's parameters are considered as fixed effects whereas the SITAR model's parameters (3) are considered as mixed (fixed effects + random effects).

The SITAR model for subjects $i = 1, 2 \ldots N$ and time points t = $1, 2 \ldots T_i$ can be specified as:

$$y_i(t) = \alpha_i + h\big((t - \beta_i)/e^{-\gamma_i}\big) + \eta_{it} \quad (5)$$

where

$y_i(t)$ = weight measured for i^{th} child at age t

t = age (time) variable (in years)

$h(t)$ = a function that describes non-linear relationship between weight and age represented using natural cubic spline curve of the weight regressed on age

The α_i, β_i and γ_i are subject-specific parameters expressed as $\alpha_i = \alpha_0 + \alpha_{1i}$, $\beta_i = \beta_0 + \beta_{1i}$, $\gamma_i = \gamma_0 + \gamma_{1i}$ where α_0, β_0, γ_0 represents fixed effects and α_{1i}, β_{1i}, γ_{1i} represents random effects. These parameters are assumed to be drawn from a multivariate normal distribution with mean 0 and variance-covariance matrix λ. The error term η_{it} follows a normal distribution with mean 0 and variance σ^2 and are independent of the child-specific random effects. α_{1i}, β_{1i} for each subject i refers to the shift parameter for y (weight) axis and the x (age) axis respectively whereas γ_{1i} refers to the scale parameter for the x (age) axis. The SITAR model's parameters α_i, β_i and γ_i are referred to as size, tempo/timing and velocity/intensity respectively where the first two parameters lead to a translation in the spline curve, and third parameter refers to a rotation for the growth curve. Based on their biological interpretability, α_i refers to a random weight intercept that adjusts for the difference in individual's mean weight. The parameter size (α_i) adjusts the average growth curve by vertically shifting it up or down. The positive or negative values of the size indicates whether the child is heavier/larger or lighter/smaller than the average weight of the sample. The parameter β_i refers to the random age intercept that adjusts for the differences in the individual's timing of the pubertal growth spurt based on the APWV. The parameter tempo (β_i) adjusts the average curve by horizontally shifting the curve left or right. The positive or negative values of the tempo indicates whether the timing of the peak weight velocity is earlier or later than the timing of peak weight velocity of the average curve. The parameter γ_i refers to the random age scale that adjusts for the differences in the individual's duration of the growth spurt (i.e. reaching the peak weight velocity). The parameter velocity (γ_i) corresponds to the shrinking and stretching of the age scale. The positive value of the velocity indicates the shrinking of the age scale which makes the curve steeper and increases the velocity leading to fast growth. The negative value of the velocity indicates the stretching of the age scale which makes the curve shallower and decreases the velocity leading to slow growth. When the random effects α_{1i}, β_{1i} and γ_{1i} are removed (equated to zero) in the model, all individuals' growth curves would be back transformed and will lie on the mean growth curve.

Figure 2.2 is from paper Cole et al.'s (2010) and provides the geometric description of the three SITAR parameters. The black solid line represents the average growth curve of the sample. The red dashed lines indicate the vertical shift in the curve (upward and downward) which is represented by size (α). The blue dashed lines indicate the horizontal shift in the curve (left or right) represented by tempo (β). The green dot-dashed lines indicate the shrinking and stretching of the curve corresponding to velocity (γ). These parameters describe how each individual's growth curve can differ from the mean curve.

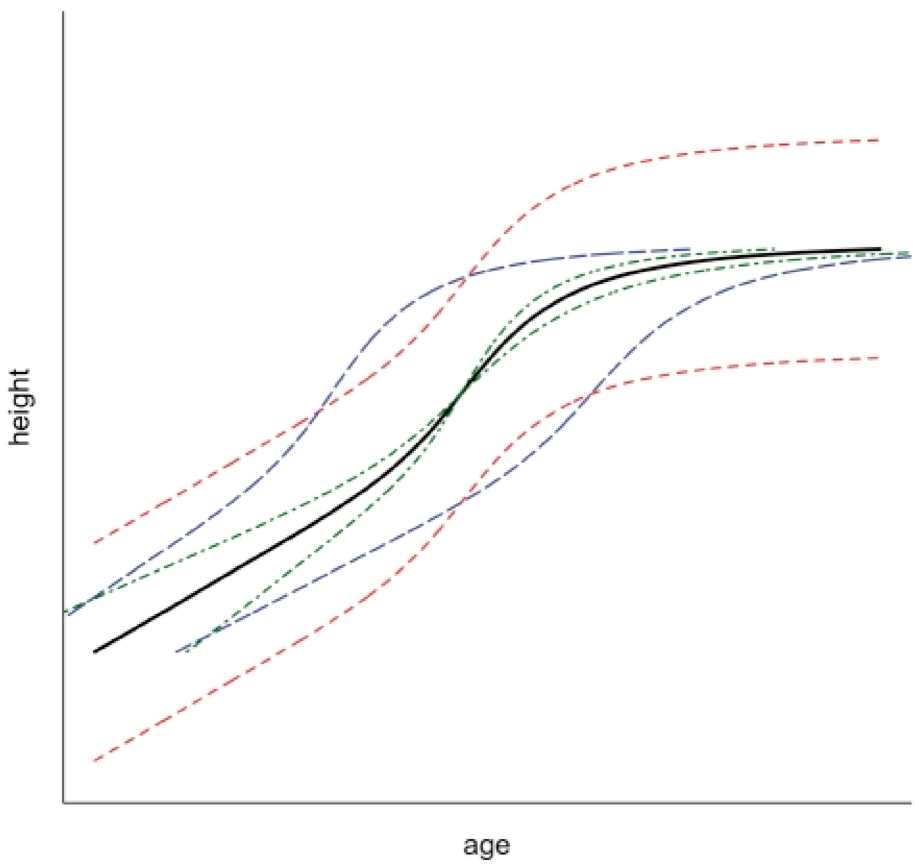

Figure 2.2: Graphical description of the SITAR model parameters from Cole et al. (2010)

2.3 Statistical analysis

All the data analyses comparing several anthropometric growth models (Jenss-Bayley and Reed models and their extensions) alongside the recently developed SITAR model to model longitudinal weight data from 6 to 15 years of age (childhood to adolescence) were separated by sex. While the Jenss-Bayley and Reed models and their extensions were conducted within the mixed effect framework, the SITAR model was a shape invariant random effects model. The variables used in this analysis included sex, age and weight of the subjects. From the initial cohort (n = 2,120), subjects with at least one non-missing weight and age observation were included in accordance with the literature (Pizzi et al., 2014). Thus, the participants (n = 323: females = 126, males = 197) with missing growth data at all seven measurement occasions were excluded from the analysis. In addition, subjects that only had either their weight or age and were missing all other data were also excluded (n = 60, females = 26, males = 34), leaving a final sample size of: 1737 subjects. The units of measurements used for the age and weight variables in this study were kilograms (kg) and years, respectively. All the statistical analyses were performed using R (Team, 2013) (version-1.1.383). All the statistical tests were conducted at 5% significance level.

Firstly, descriptive statistics such as means, standard deviations and range were calculated for weight at each time point of interest for females and males. T-tests were then conducted to compare mean weight among females and males at birth and at each measurement occasion (at ages 6, 7, 8, 10, 12, 13 and 15). T-tests were also performed to compare weight change velocity (kg/year) among females and males at 3 different time intervals (6-10, 10-12 and 12-15 years). Each child's weight was converted to weight-for-age z-scores according to WHO growth curves for Canada (Rodd, Metzger, & Sharma, 2014). Also, mean weight z-scores for females and males were calculated at each time point. T-tests were also used to compare any significant differences in mean weight-for-age z-scores between females and males at each time point of interest. Observed weight growth curves of a random selection of females and males separately were also plotted. The wide form data set was then converted to long form to fit mixed effect growth models (Fitzmaurice et al., 2012).

Secondly, the five anthropometric growth models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, Adapted Jenss-Bayley, and SITAR) were fitted using mixed effect modelling framework. The functions of the predictor age such as natural logarithm of age $ln(age)$, square of the age $(age)^2$, inverse of age $(1/age)$ and inverse of age square $(1/(age)^2)$ were also calculated to fit these growth weight models. The weight data were unbalanced as the weight measurements were not collected at fixed time points for every individual and also due to lost to follow-up. The implications of this on the results are described in the discussion section.

The Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley models were fitted with untransformed weight data. Natural logarithmic transformations of the weight observations were also considered. The results obtained from the untransformed weight modelling were then compared with transformed weight results (Pizzi et al., 2014). The SITAR model was fitted using a natural cubic regression B-spline curve $f(t)$. The specification of the degrees of freedom implies the placement of the knots of the spline curve $f(t)$ at the quantiles of the age distribution. The selection of the degrees of freedom depends upon the number of available weight measurements over the age timescale. Different degrees of freedom were also tried. Firstly, the SITAR models were fitted with all fixed and random effects of the parameters α, β and γ. The different alternatives of the models were also carried out on the fixed effects values by fixing either $\beta_0 = 0$ and $\gamma_0 = 0$ together or $\beta_0 = 0$ only or $\gamma_0 = 0$ only. These alternative constraints were performed with the untransformed and natural logarithm transformation of both weight and age scales (Pizzi et al., 2014).

The estimation of the growth models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley) were conducted by simple non-linear regression using the nls (non-linear least square) function in R without random effects to obtain starting values for the parameters of the growth models. These growth models were then later fitted by the nlme function (non-linear mixed effects) in R (Pizzi et al., 2014) using the estimates obtained from the nls function as the starting values for the growth parameters along with the random effects of the parameters (Pinheiro et al., 2017). The SITAR model was fitted by using the SITAR function (based on nlme function) in the SITAR package (version-1.0.9) provided by R environment (Cole & Cole, 2017). Maximum likelihood of estimation was used as the method of estimation while fitting the models in the nlme and sitar functions. Based on the literature (Pizzi et al., 2014), the covariance structure of the within subject residuals and the random effects of the growth parameters were assumed as independent and unstructured respectively. Diagnostic testing was performed to assess the assumptions of the fitted models by plotting residual plots and normal quantile plots.

In comparing models to one another, the log likelihood ratio test (for nested models) and the Akaike information criteria (AIC) (Sakamoto, Ishiguro, & Kitagawa, 1986) and Bayesian information criteria (BIC) (Schwarz, 1978) (for non-nested models) were used. Among the growth models, the model with the lowest AIC, BIC and Residual Standard Deviation (RSD) was preferred over the other models. In order to find the best model within each theory (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley) the untransformed weight model was compared with the log transformed weight model. Within each theory, the untransformed weight and log transformed weight models were non-nested models therefore they were compared in terms of AIC, BIC and minimum RSD. Within the SITAR theory, the models with different weight and age scales (untransformed and log transformed) were fitted with all the fixed and random effects first and then with the alternative restrictions imposed on the fixed effects. In order to determine the best model within the SITAR theory, these models were then compared in terms of AIC, BIC and RSD. The best model selected from Jenss-Bayley was compared with the best model from Adapted Jenss-Bayley. Similarly, the best model selected from Reed 1^{st} order was compared with the best model selected from Reed 2^{nd} order. The best models selected from each one of the theories were then compared with one another. When the weight was transformed, the corrected or adjusted AICs and BICs were calculated. Also, the Peak Weight Velocity (PWV) and Age at Peak Weight Velocity (APWV) were estimated from the SITAR models when possible.

Plots of population level predicted weight growth curves and growth velocity curves obtained from the fitted fixed effects growth models were also examined. The average predicted weight at selected ages were also calculated from the five fitted models.

2.4 General mixed effect model building procedure

The following steps were conducted to build a final model for Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order and Adapted Jenss-Bayley models:

Step 1: The growth models were first fitted for untransformed observed weight data. The modelling procedure started by first fitting these anthropometric models as a simple non-linear regression model (fitting the data with fixed effects only). The models required appropriate or good initial values for the estimation of their parameters in order to allow the models to converge to a solution quickly. Thus, the starting values were chosen based on the data and also through trial and error. Some of the starting values that were chosen for the modelling lead to the non-convergence of the models. Those starting values that lead to the convergence of the models had negative intercepts for Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models. Therefore, it was required to center the age in order to have interpretable intercepts. The age was left centered at age 5. Age could also be centered around mean age for females (female's age - 10.14) and males (male's age - 10.12) for original Jenss-Bayley and Adapted Jenss-Bayley models but not for Reed 1^{st} and 2^{nd} order models. This happened due to the fact that the latter models have a logarithm term $ln(age)$ and the logarithm of negative values are not defined. Thus, in order to be consistent in the analyses, age was left centered at age 5 for Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} and 2^{nd} order models. The growth models were also fitted for natural logarithmic transformation of weight scale and untransformed age in order to be consistent with the SITAR model

Step 2: On trying different starting values for the model parameters, many models failed to converge. However, specifying starting values of 1-15 (for the intercept), and 1-4 (for the slope) resulted in coverging with similar estimates for parameters and producing similar standard errors.

Step 3: The models were then fitted as non-linear mixed effect models which further allowed the incorporation of the random effects of the average growth parameters estimates. The estimated values obtained from fitting the model as a non-linear regression model (step 2) were used as the initial estimates for these mixed effect models.

Step 4: The random effects of the parameters were added systematically to the fixed effect models in accordance to the literature (Pinheiro & Bates, 2000). The models were checked for convergence after adding each random effect. Significance testing of each random effect in a mixed model (compared to the model without the random effect) was also conducted using a likelihood ratio test. The fitted values obtained after the addition of each random effect to the model were used as the starting values for the model when the next random effect of the parameter was added.

Chapter 3

Results

3.1 Descriptive analysis

All the data analyses comparing weight growth characteristics at birth and specifically from 6 to 15 years of age (middle childhood to adolescence) were stratified by sex for this research study. In the QLSCD cohort (n = 2,120), approximately 49% (1040/2120) were females and 51% (1080/2120) were males. The analytic sample that was used in this research study consisted of n = 1,737 participants (females = 888, males = 849) (after data exclusions as specified previously). In this study, the age of females ranged between approximately 68.5 (at baseline) to 188 (at last follow-up) months and males ranged between approximately 68.4 to 188 months. The average number of weight measures in females and males were approximately 5 with a standard deviation of 1.96 and 2.03 respectively. From Table 3.1, the number of subjects with complete data (all seven measurements for an individual at ages 6, 7, 8, 10, 12, 13 and 15) for females were n = 378 (42.57% of 888) and males were n = 309 (36.40% of 849).

Table 3.1: Number of weight measurements per child

Measures	N Females	N Males	% Females	% Males
1	72	78	8.11%	9.19%
2	50	51	5.63%	6.01%
3	45	80	5.07%	9.42%
4	64	74	7.21%	8.72%
5	87	93	9.80%	10.95%
6	192	164	21.62%	19.32%
7	378	309	42.57%	36.40%

Table 3.2 below provides the descriptors of weight for females and males at birth and each data collection wave from 6 to 15 years of age. The average birth weight of females was 3.37 kg with a standard deviation of 0.48 kg and ranging between 1.09 to 4.97 kg. The average birth weight of males was 3.44 kg with a standard deviation of 0.52 kg and ranging between 0.99 to 5.26 kg. Average body weight ranged between 21.68 - 56.85 kg in females and 22 - 62.86 kg in males. Comparisons of mean weight by sex were conducted at birth and at each measurement occasion (from 6 to 15 years). It was noticed that at birth, females were a little heavier than males and the difference was significant (p-value = 0.0006). The difference in weight between females and males was not significant (p-value >0.05) from age 6 to 10 years except at the age of 7 (p-value = 0.04) with a difference of approximately 0.5 kg more in males. Around age 12, there was a significant difference in mean weight between females and males (p-value <0.05) indicating that there was a rapid increase in females' average weight and they tended to be heavier than males. Females continued to have a little more body weight than males at age 13 but the difference was not significant (p-value = 0.86). There was an increase in males' average body weight compared to females' at approximately 15 years of age with a difference of approximately 6 kg. This difference was significant (p-value <0.05). The weight change velocity did not show any significant difference (p-value = 0.1052) between females and males from 6 to 10 years. The difference was found to be significant (p-value <.0001) between 10 to 12 years when the females weight change velocity (5.65 kg/year) was higher than males (4.81 kg/year) and from 12 to 15 years when the males weight change velocity (5.58 kg/year) was higher than females (3.12 kg/year). Each child's weight at each time point was calculated and converted to age and sex specific z-scores. The mean weight z-scores for females and males were above 0 indicating that the children in this study were heavier than the reference population mean

at all time points. There were no significant differences between the mean weight z-scores of females and males from 6 to 10 years of age (p-value >0.05), but significantly differed between the sexes at ages 12, 13 and 15 years (p-value <0.05).

Table 3.2: Characteristics of QLSCD females (F) and males (M) at birth and from 6 to 15 years of age (Weight and Age over time)

Weight(kg)	**F Range**	**M Range**	**F Mean(SD)**	**M Mean(SD)**	**p-value**
birth	1.09-4.97	0.99-5.26	3.37(0.48)	3.44(0.52)	0.0006
6	14.55-43.18	13.18-48	21.68(3.72)	22.00(3.82)	0.15
7	15-52	15-58	24.25(4.63)	24.75(4.78)	0.04
8	13.64-57	17.55-63.64	27.44(5.65)	27.77(5.74)	0.28
10	21.6-82.2	21.6-88	36.46(8.28)	36.23(8.43)	0.63
12	26.8-111.4	25-113	47.54(11.37)	45.96(11.78)	0.01
13	31.6-122.2	27.4-124.5	52.67(11.60)	52.54(13.71)	0.86
15	32.85-135	30-121.5	56.85(11.96)	62.86(13.84)	<.0001
WCV(kg/year)					
6-10 years	(-1.05,10.44)	(-0.1,10)	3.71(1.38)	3.56(1.46)	0.1052
10-12 years	(-1.4,16)	(-10.93,16.3)	5.65(2.32)	4.81(2.55)	<.0001
12-15 years	(-9.15,26.17)	(-7.2,23.53)	3.14(2.84)	5.72(2.54)	<.0001
Weight z-scores					
6	(-2.66,5.09)	(-3.9,6.08)	0.26(1.01)	0.27(1.16)	0.85
7	(-3.19,4.46)	(-3.7,6.35)	0.26(1.05)	0.28(1.20)	0.74
8	(-4.16,4.10)	(-3.16,5.57)	0.28(1.10)	0.31(1.25)	0.67
10	(-2.46,3.53)	(-2.77,4.50)	0.43(1.03)	0.55(1.14)	0.05
12	(-2.44,4.13)	(-2.92,4.38)	0.37(1.03)	0.50(1.14)	0.03
13	(-2.45,4.48)	(-3.08,4.48)	0.35(1.01)	0.49(1.16)	0.03
15	(-3.49,4.79)	(-3.93,4.04)	0.18(1.04)	0.32(1.16)	0.02

WCV: Weight Change Velocity
SD: Standard Deviation
N's for the variable weight ranged from 599, 774, 703, 672, 689, 661, 698 in females at ages 6, 7, 8, 10, 12, 13 and 15, respectively
N's for the variable weight ranged from 536, 701, 648, 595, 645, 569, 634 in males at ages 6, 7, 8, 10, 12, 13 and 15, respectively

Plots of observed weight growth trajectories of a random sample (65 subjects in total) stratified by sex with an average weight line [in red] at 6, 7, 8, 10, 12, 13 and 15 years are shown in Figure 3.1. The females' plot shows that the mean weight was increasing approximately linearly from 6 to 8 years of age followed by a rapid increase in weight until age 13 (approximately). Females' weight was growing continually after age 13 but at a slower rate. The males' plot shows a similar pattern as females where the mean weight was approximately constant from 6 to 8 years of age with an increase in weight that further continued until age 12 (approximately). There was a rapid increase in males' weight after age 12 and was growing continually until age 15 at an increasing rate as compared to females'.

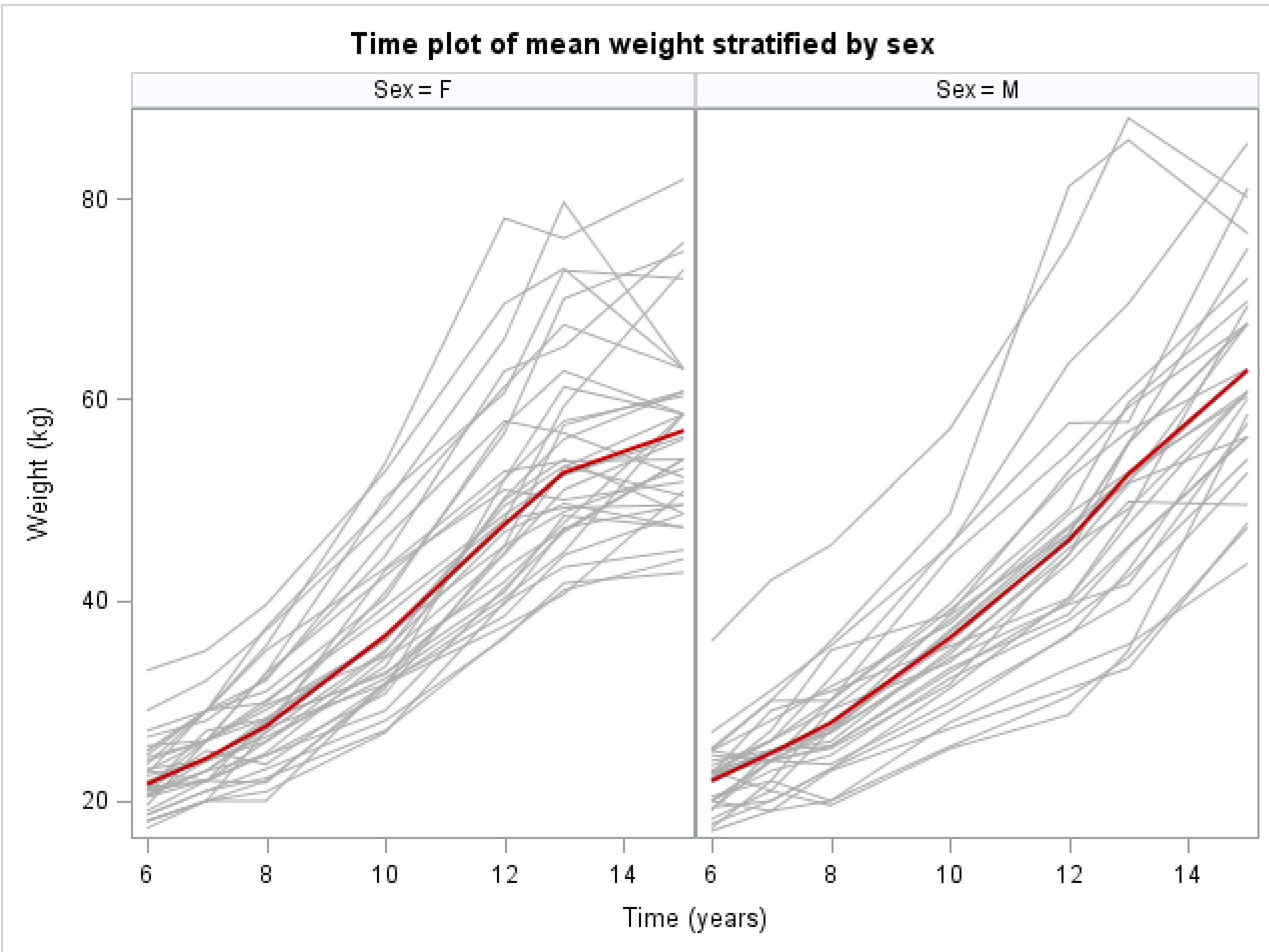

Figure 3.1: Observed weight growth curves of random selection of females and males

3.2 Model fitting results

3.2.1 Jenss-Bayley model

The Jenss-Bayley mixed effects model for females converged. The results are shown in Table 3.3. The model converged when the random effect a_{1i} of the intercept a_0 was added. The model further converged when the random effect b_{1i} of the slope b_0 was also added. However, the addition of random effects c_{1i} and d_{1i} of the parameters c_0 and d_0 lead to the non-convergence of the model. Therefore, the final Jenss-Bayley model for females consisted of fixed effects a_0, b_0, c_0, d_0 for all the parameters a_i, b_i, c_i and d_i including only the random effects a_{1i} and b_{1i} of the intercept a_0 and slope b_0 respectively.

For females, all four estimated fixed effect parameters were found to be significant in the model (p-value <0.05). These fixed effects represent the average growth curve for the females within the sample. The age was left centered at age 5, therefore the females mean weight at 5 years was a_0 - e^{c_0} (14.5 kg when the other parameters were held constant). The average rate of growth during childhood and adolescence for females was 4.57 kg per year. The random intercept and random slope in the females fitted Jenss-Bayley model indicated that each subject had their own individual estimates of the intercept and rate of growth of their weight growth curves from middle childhood to adolescence. Therefore, the standard deviations around the starting point and growth rate of the average weight curve for females were 3.3 kg and 1.09 kg per year respectively. The term e^{c_0} i.e., $e^{(-14.87)}$ corresponds to $3.48 * 10^{-7}$ implying that the vertical distance between the intercept of the distance curve and the intercept of its asymptote was nearly 0. This indicated that the females average growth curve was following its asymptote very closely. The Jenss-Bayley mixed effect model was incapable of finding the unique estimates for the deceleration term for each individual in the age range (6 to 15 years). This further indicated that the magnitude of deceleration term was the same for all the females in the same time interval.

In contrast to females, the Jenss-Bayley model failed to converge when fitted on the males' data from age 6 to 15 years (Table 3.4). The reason behind this non-convergence could be the fact that the model may be over parametrized for the males data in the age range (6 to 15 years) as compared to Jenss-Bayley's original conceptualization to model growth between birth and 6 years. In support of this reason, it was also observed that when the exponential component of the Jenss-Bayley equation was not included in model fitting, the model converged with valid estimates of the intercept and slope parameters (fixed+random). This may imply that the males' follow constant growth until they start their pubertal spurt which might start later in males. However, it is possible that some are starting puberty by the age of 13 or 14 where it affects their weight, and others are not which could have strongly affected fitting the model and estimating the solution. Also, the model fails to capture the end part of the growth spurt when the weight velocity starts decreasing.

3.2.2 Reed 1^{st} order model

The Reed 1^{st} order mixed effect models converged for both females and males having random intercept $\hat{a}_i{}'$ and random slope $b_i^{'}$. The results are shown in Tables (3.3 and 3.4) respectively. The models did not converge when the random effects $c_{1i}^{'}$ and $d_{1i}^{'}$ of the deceleration parameters $c_0^{'}$ and $d_0^{'}$ were added. These models adjusted for the differences in the individual's intercept and slope of the linear asymptote with the same magnitude of decelerating rate of growth for both females and males.

The estimates of the Reed 1^{st} order growth parameters for males provided better and more logical numerical estimates than the females. The fixed effect estimates of the intercept $a_0^{'}$ and slope $b_0^{'}$ of the asymptote for males were higher than females whereas $c_0^{'}$ and $d_0^{'}$ estimates of males were lower than the females. The fixed effect parameters for males were all found to be significant (p-value <0.05). Since the Reed 1^{st} order models contain a logarithmic term, it was not possible to interpret the average weight at 5 years of age. Thus, for males, the average or predicted weight at 6 years of age was 21.66 kg. For each unit increase in age the weight would increase by 7.29 kg per year. The overall model for females predicted 21.13 kg at 6 years of age with an increment of approximately 3 kg per year. The decelerating parameters were found to be significant and having no random effects of these parameters implies the same deceleration growth rate for females and males during childhood and puberty phase. The corresponding SD's of the random effects $a_{1i}^{'}$ was higher and $b_{1i}^{'}$ was lower in females than males.

3.2.3 Reed 2^{nd} order model

The results for both females and males are shown in Tables 3.3 and 3.4 respectively. Similar to other models, the Reed 2^{nd} order models also converged under the mixed effect framework for both sexes. In particular, the models' convergence was also achieved for both females and males when the random effects of the intercept $a_0^{''}$ and $b_0^{''}$ were added. The models also converged after the addition of the random effects $e_{1i}^{''}$ of the fifth parameters $e_0^{''}$ for both females and males. However, the models failed to converge when the random effects $c_{1i}^{''}$ and $d_{1i}^{''}$ of the decelerating rate of growth parameters $c_0^{''}$ and $d_0^{''}$ were added.

Like Reed 1^{st} order, Reed 2^{nd} order model for males also provided more reasonable parameter estimates than females. The estimated fixed effects $a_0^{''}$, $b_0^{''}$ and $e_0^{''}$ were higher in males than females whereas estimated $c_0^{''}$ and $d_0^{''}$ were higher in females than males. The mean weight at 6 years for males was 21.61 kg with a linear slope of 7.82 kg per year. Even after centering the data, the model for females estimated a negative value of the intercept $a_0^{''}$. The average weight for females at 6 years of age was 22.44 kg with mean slope of -0.62 kg per year. The SD's of the random effect $a_{1i}^{''}$ was higher in females than males followed by $b_{1i}^{''}$ and $c_{1i}^{''}$ were higher in males than females.

3.2.4 Adapted Jenss-Bayley model

For both females and males, the Adapted Jenss-Bayley mixed effect models converged. Tables 3.3 and 3.4 shows the results of females and males respectively. The models also converged after the systematic addition of the random effects $a_{1i}^{'''}$ and $b_{1i}^{'''}$ of the intercept $\hat{a_0}^{'''}$ and the slope $b_0^{'''}$. The randomly varying intercepts and slopes indicated that every child has its own intercept of their growth curve and linear rate of growth. However, the models failed to converge when the random effects $c_{1i}^{'''}$ and $d_{1i}^{'''}$ of the deceleration parameters $e^{(c_0^{'''}+d_0^{'''}t)}$ were added. Addition of random effects $e_{1i}^{'''}$ of the parameters $e_0^{'''}$ (p-value <0.05) were found to be significant in females and males. This indicates that the addition of the fifth parameter in Adapted Jenss-Bayley provided a significant improvement over the four parameter Jenss-Bayley model. Thus, the final Adapted Jenss-Bayley models consisted of fixed effects $a_0^{'''}$, $b_0^{'''}$, $c_0^{'''}$, $d_0^{'''}$ and $e_0^{'''}$ including the random effects $a_{1i}^{'''}$, $b_{1i}^{'''}$ and $e_{1i}^{'''}$ of the intercept $a_0^{'''}$, slope $b_0^{'''}$ and velocity $e_0^{'''}$ (at the start of puberty) for both females and males.

The fixed effect estimates of the intercept of the asymptote $a_0^{'''}$, deceleration parameter $c_0^{'''}$ and onset puberty velocity $e_0^{'''}$ for the females were higher than males whereas the slope $b_0^{'''}$ and deceleration parameter $d_0^{'''}$ estimates were higher in males than females. At 5 years of age, the predicted weight $(a_0^{'''} - e^{c_0^{'''}})$ for females was 20.54 kg and for males was 19.63 kg when the other parameters were held constant. The variances of the mean weight and slope for females were 11.56 kg and 10.56 kg per year and for males were 10.69 kg and 7.89 kg per year respectively. These variances indicate between-individual differences in growth trajectories (in varying intercepts and varying growth rates) from middle childhood to adolescence. The model also indicates that it was capable of finding specific estimates of the increase in velocity for every individual that occurs at the onset of puberty. The models for females and males did not estimate random effects of the parameters in the exponential function indicating that the children experience the same deceleration rate in growth at the same time. This model accounted for adjusting the individual growth curve differences with respect to random intercept $a_i^{'''}$, random slope $b_i^{'''}$ and random pubertal velocity $e_i^{'''}$ when the adolescent spurt starts. The corresponding random effects SD's for the parameters $a_0^{'''}$ and $e_0^{'''}$ were quite similar across genders but for the slope it was higher in females than males.

Table 3.3: Estimated parameters for fixed effects and random effects SD's of Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley models for females fitted on the original weight scale

Model	**Parameters**	**FE**	**SE**	**p-value**	**95% CI of FE**	**RE(SD)**	**95% CI of RE**
JB	a_0	14.5	0.17	<0.0001	(14.16,14.83)	3.3	(3,3.63)
	b_0	4.57	0.05	<0.0001	(4.48,4.66)	1.09	(1.02,1.16)
	c_0	-14.87	2.52	<0.0001	(-19.81,-9.94)		
	d_0	1.59	0.24	<0.0001	(1.11,2.07)		
R1	$a_0^{'}$	0.04	1.26	0.9693	(-2.41,2.51)	3.16	(2.86,3.49)
	$b_0^{'}$	2.97	0.15	<0.0001	(2.67,3.28)	1.09	(1.03,1.16)
	$c_0^{'}$	11.55	1.09	<0.0001	(9.41,13.68)		
	$d_0^{'}$	18.12	1.44	<0.0001	(15.30,20.94)		
R2	$a_0^{''}$	-67.53363	0.11	0.5939	(-77.11,-57.96)	4.3	(3.91,4.74)
	$b_0^{''}$	-0.62629	0.01	<0.0001	(-1.20,-0.05)	1.12	(1.06,1.19)
	$c_0^{''}$	51.51071	0.07	<0.0001	(45.65, 57.37)		
	$d_0^{''}$	133.66299	0.18	<0.0001	(117.59,149.74)		
	$e_0^{''}$	-43.0652	0.07	<0.0001	(-48.95,-37.18)	1.82	(1.37,2.43)
AJB	$a_0^{'''}$	20.95	0.56	<0.0001	(19.85,22.05)	3.4	(3.03,3.82)
	$b_0^{'''}$	0.61	0.18	0.001	(0.25,0.97)	3.25	(3.04,3.46)
	$c_0^{'''}$	-0.9	0.76	0.234	(-2.42,0.59)		
	$d_0^{'''}$	0.44	0.06	<0.0001	(0.33,0.55)		
	$e_0^{'''}$	0.62	0.07	<0.0001	(0.48, 0.75)	0.27	(0.25, 0.27)

JB: Jenss-Bayley, R1: Reed 1^{st} order, R2: Reed 2^{nd} order, AJB: Adapted Jenss-Bayley
FE: Fixed Effects, SE: Standard Error, RE: Random Effects, SD: Standard Deviation,
95% CI of FE: 95% Confidence Interval of Fixed Effects,
95% CI of RE: 95% Confidence Interval of Random Effects,
The best way to read the results is as follows (using JB model as an example):
In the final model, there were four fixed effects estimates a_0, b_0, c_0 and d_0 but only two random effects estimates of a_0 and b_0 due to convergence isssues.

Table 3.4: Estimated parameters for fixed effects and random effects SD's of Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley models for males fitted on the original weight scale

Model	Parameters	FE	SE	p-value	95% CI of FE	RE(SD)	95% CI of RE
JB				Failed to converge			
R1	$a_0^{'}$	26.59	1.11	<0.0001	(24.41,28.76)	2.86	(2.58,3.18)
	$b_0^{'}$	7.29	0.14	<0.0001	(7.11,7.66)	1.39	(1.31,1.47)
	$c_0^{'}$	-15.87	0.96	<0.0001	(-17.75,-13.98)		
	$d_0^{'}$	-12.22	1.27	<0.0001	(-14.69,-9.73)		
R2	$a_0^{'}$	34.89	4.42	<0.0001	(26.2,43.55)	4	(3.61,4.41)
	$b_0^{'}$	7.82	0.27	<0.0001	(7.29,8.35)	1.45	(1.37,1.54)
	$c_0^{'}$	-20.72	2.71	<0.0001	(-26.02,-15.41)		
	$d_0^{'}$	-26.53	7.41	<0.0001	(-41.06,-12)		
	$e_0^{'}$	5.43	2.71	0.45	(0.13,10.74)	2.15	(1.73,2.67)
AJB	$a_0^{'''}$	19.63	0.22	<0.0001	(19.19,20.07)	3.27	(2.84,3.76)
	$b_0^{'''}$	1.75	0.14	<0.0001	(1.47,2.03)	2.81	(2.61,3.02)
	$c_0^{'''}$	-18.01	4.43	<0.0001	(-26.71,-9.31)		
	$d_0^{'''}$	1.87	0.43	<0.0001	(1.03,2.70)		
	$e_0^{'''}$	0.28	0.01	<0.0001	(0.25,0.31)	0.22	(0.20,0.24)

JB: Jenss-Bayley, R1: Reed 1^{st} order, R2: Reed 2^{nd} order, AJB: Adapted Jenss-Bayley
FE: Fixed Effects, SE: Standard Error, RE: Random Effects, SD: Standard Deviation
95% CI of FE: 95% Confidence Interval of Fixed Effects
95% CI of RE: 95% Confidence Interval of Random Effects
The best way to read the results is as follows (using R1 model as an example):
In the final model, there were four fixed effects estimates $a_0^{'}$, $b_0^{'}$, $c_0^{'}$ and $d_0^{'}$ but only two random effects estimates of $a_0^{'}$ and $b_0^{'}$ due to convergence isssues.

3.2.5 SITAR model

The SITAR models were fitted by allowing different scales (untransformed and natural logarithm transformation) for both weight and age variables (Cole et al., 2010; Pizzi et al., 2014; Riddell et al., 2017). In order to calculate the adjusted AICs and BICs for the log transformed weight models (Box & Cox, 1964; Akaike, 1978; Cole & Cole, 2017), the formulas that were used are as follows:

Adjusted AIC = original AIC + $(2 * \Sigma log(weight))$

Adjusted BIC= original BIC + $(2 * \Sigma log(weight))$

The parameters of the common spline curve were fitted as fixed effects. The number of internal knots (degrees of freedom) for the spline curve were chosen based on the number of available weight measurements for the present study. Pizzi and his colleagues (2014) selected 3 degrees of freedom for 6 weight measurements. Therefore, for this study 3 degrees of freedom were chosen for 7 weight measurements to fit and compare different SITAR models for females and males. The SITAR models were first fitted with all three parameters (size, tempo and velocity) as both fixed and random effects (Model 1). When the SITAR parameters were fitted as fixed and random effects in the models, non-convergence issues were observed. Therefore, to achieve convergence, the alternative restrictions on the fixed effects values were also examined by fixing either $\beta_0 = 0$ and $\gamma_0 = 0$ (Model 2) together or just $\beta_0 = 0$ (Model 3) or just $\gamma_0 = 0$ (Model 4) (Cole et al., 2010; Pizzi et al., 2014; Riddell et al., 2017).

For females, the four models (1, 2, 3 and 4) were fitted with 3 degrees of freedom. The results are shown in Table 3.5. It was observed that models with log transformed weight scale performed better than the untransformed weight scale in terms of AICs and BICs. In particular, models with log transformed weight and untransformed age performed better than the models with log transformed weight and log transformed age. Thus, among different log transformed weight and untransformed age models, Model 4 ($\gamma_0 = 0$) performed the best with the lowest values of AIC, BIC and RSD. The random effect of the parameter size produced an RSD = 2.98. When the random effect of the parameter velocity was added, the RSD was reduced to 2.51. Further by adding the random effect of the tempo, the RSD was reduced to 1.95. The model explained 91.64% of variations in the weight. Using this model, it was possible to estimate valid APWV and PWV.

Table 3.5: Estimated parameters of random effects from different specification of the SITAR models for females

Model	Random effects(SD) α	β	γ	AIC	BIC	APWV	PWV	RSD
Model1:$\alpha_0 \neq$0,$\beta_0 \neq$0,$\gamma_0 \neq$0								
Weight and Age	8.68	1.11	0.42	27524.26	27608.44	10.82	6.01	2.52
Weight and Log(Age)				Failed to converge				
Log(Weight) and Age	0.19	0.50	0.15	25473.44	25557.62	11.73	5.8	2.08*
Log(Weight) and Log(Age)	0.16	0.10	0.21	25555.31	25639.5	10.96	5.35	2.05*
Model2:β_0=0 and γ_0=0								
Weight and Age	6.24	1.05	0.39	28024.65	28095.88	10.35	5.76	2.94
Weight and Log(Age)	3.21	0.12	0.33	27984.67	28055.9	9.78	5.54	2.94
Log(Weight) and Age	0.16	1.01	0.19	25556.21	25627.44	10.91	6.13	2.06*
Log(Weight) and Log(Age)	0.14	0.10	0.20	25898.26	25969.47	10.34	5.44	2.22*
Model3:β_0=0								
Weight and Age	6.47	1.14	0.41	27887.11	27964.82	10.43	5.46	2.85
Weight and Log(Age)	3.30	0.12	0.33	27986.3	28064	9.68	5.36	2.96
Log(Weight) and Age	0.17	0.82	0.20	25419.27	25496.97	11.28	5.39	2.01*
Log(Weight) and Log(Age)	0.13	0.09	0.20	25856.49	25934.19	10.46	5.11	2.24*
Model4:γ_0=0								
Weight and Age	8.67	1.13	0.41	27373.1	27450.8	10.88	5.89	2.44
Weight and Log(Age)	3.8	0.11	0.36	27880.25	27957.96	10.00	5.81	2.87
Log(Weight) and Age	**0.17**	**0.94**	**0.18**	**25307.99**	**25385.69**	**11.43**	**6.00**	**1.96***
Log(Weight) and Log(Age)	0.17	0.08	0.2	25338.92	25416.62	10.84	5.73	2.00*

The best model is highlighted in bold
SD: Standard Deviation, AIC: Akaike Information Criteria, BIC: Bayesian Information Criteria
APWV: Age at Peak Weight Velocity, PV: Peak Velocity, RSD: Residual Standard Deviation
*RSD obtained by multiplying geometric mean of females' weight

On the other hand, for males with 3 degrees of freedom, none of the models converged when the models were fitted with all fixed and random effects of the parameters size, tempo and velocity (Model 1) shown in Table 3.6. Modelling using alternative constraints on fixed effects, only the models with untransformed weight and log transformed age (models 2 and 3) converged plus only a single model with log transformed weight and untransformed age of Model 4. Out of these models, the models with untransformed weight and untransformed age of models (2 and 4) did not provide valid estimates of APWV and PWV.

In comparing all the models (which converged with 3 degrees of freedom) to one another, similarly to the females data the model with log transformed weight and untransformed age of $\gamma_0 = 0$ (Model 2) also fitted the best based on minimum AIC, BIC and RSD values. The random effect of the parameter size produced an RSD = 3.21. When the random effect of the parameter tempo was added, the RSD was reduced to 3.08. Further, the addition of the random effect of the velocity, reduced RSD to 2.14. The model explained 91.41% of variations in the weight.

Table 3.6: Estimated parameters of random effects from different specification of the SITAR models for males

	Random Effects							
Model	α	β	γ	**AIC**	**BIC**	**APWV**	**PWV**	**RSD**
Model1:$\alpha_0 \neq$**0,**$\beta_0 \neq$**0,**$\gamma_0 \neq$**0**								
Weight and Age				Failed to converge				
Weight and Log(Age)				Failed to converge				
Log(Weight) and Age				Failed to converge				
Log(Weight) and Log(Age)				Failed to converge				
Model2:β_0**=0 &** γ_0**=0**								
Weight and Age	4.47	2.1	0.27	24969.17	25039.28	15.6	5.86	2.72
Weight and Log(Age)	3.69	0.21	0.28	24818.94	24889.04	13.9	6.48	2.57
Log(Weight) and Age				Failed to converge				
Log(Weight) and Log(Age)				Failed to converge				
Model3:β_0**=0**								
Weight and Age	5.32	2.44	0.24	24892.04	24968.51	14.97	5.61	2.79
Weight and Log(Age)	4.22	0.22	0.29	24750.68	24827.16	12.69	6.54	2.47
Log(Weight) and Age				Failed to converge				
Log(Weight) and Log(Age)				Failed to converge				
Model4:γ_0**=0**								
Weight and Age	0	1.46	0.29	26173.34	26249.82	7.45	4.57	3.37
Weight and Log(Age)	3.87	0.22	0.29	24784.91	24861.38	12.89	6.47	2.50
Log(Weight) and Age	**0.17**	**1.45**	**0.19**	**23382.68**	**23459.16**	**13.66**	**6.29**	**2.14***
Log(Weight) and Log(Age)				Failed to converge				

The best model is highlighted in bold
SD: Standard Deviation, AIC: Akaike Information Criteria, BIC: Bayesian Information Criteria
APWV: Age at Peak Weight Velocity, PV: Peak Velocity, RSD: Residual Standard Deviation
*RSD obtained by multiplying geometric mean of males' weight

From the best fitted SITAR models for females and males, it was observed that the estimated SD's of the random effects size and velocity did not vary substantially across genders but SD of the random effect tempo was found to be higher in males than females.

3.2.5.1 Interpretations of the best fitted SITAR model parameters

For females, the size was measured in kg, tempo in years, and velocity in fractional units. Thus, when the velocity was multiplied by 100, it can be interpreted as a percentage difference from the mean curve. The best fitted model for females was log weight transformed and untransformed age, therefore exponentiating SD of size (0.17) gave an SD of 1.19 kg. The SD's of 1.19 kg for size, 0.94 years for tempo, and 18% for velocity implies that the females who deviate from the average growth curve had sizes within 2.38 kg of mean size, tempos within 1.88 years of mean tempo, and velocity within 36% of mean velocity (as random effects have means 0). The negative correlation between size and tempo (r = -0.10) indicate that the females with heavier weight tend to enter puberty earlier and have earlier APWV. The positive correlation between size and velocity (r = 0.55) suggest that females with heavier weight will experience fast growth velocities indicating that the slope during puberty will be steep. The negative correlation between tempo and velocity (r = -0.51) indicate that females with early puberty have fast growth velocity.

Similarly, like females, the best fitted model for males was also log weight transformed and untransformed age. Therefore, exponentiating SD of size (0.16) gave an SD of 1.17 kg. The SD's of 1.17 kg for size, 1.45 years for tempo, and 19% for velocity implies that the males whose growth curves differs from the average growth curve had sizes within 2.34 kg of mean size, tempos within 2.90 years of mean tempo, and velocity within 38% of mean velocity (as random effects have means 0). The positive correlation between tempo and size (r=0.55)indicate that the males who will enter the puberty later in life are heavier. However, males entering puberty earlier have the largest peak weight velocity as indicated by the negative correlation between tempo and velocity (r=-0.51).

3.3 Diagnostic testing

To examine the assumptions of the fitted models, the diagnostic testing of the residuals was performed. The plot of the standardized residuals against fitted values and standardized residuals against age were used to assess the assumption of the constant variance of the residuals and also examined which growth model was appropriate for the observed data. The normal probability plots were used to assess the normality of the residual errors obtained from each fitted model.

The males residual plots for the Jenss-Bayley model were not produced due to non-convergence of the model. For both the genders, the scatter plots of standardized residuals against fitted values (Figures 3.2 and 3.4) and standardized residuals against age (Figures 3.3 and 3.5) shows that the SITAR model fitted the observed data the best as compared to the other models. The standardized residuals of the SITAR models have constant variance as they were randomly centered around zero and were very close to the reference line passing through zero in comparison to the other models. In the case of females, the standardized residuals of Jenss-Bayley, Reed 1^{st} order and Reed 2^{nd} order models did not provide a good fit to the study data as error variances were increasing with the increasing age. The Adapted Jenss-Bayley plot provided a better fit than Jenss-Bayley, Reed 1^{st} order and Reed 2^{nd} order plots but not as good as the SITAR model plot. These scatter plots also did not suggest any systematic pattern of the standardized residuals which in return satisfied the assumption of the independence of errors.

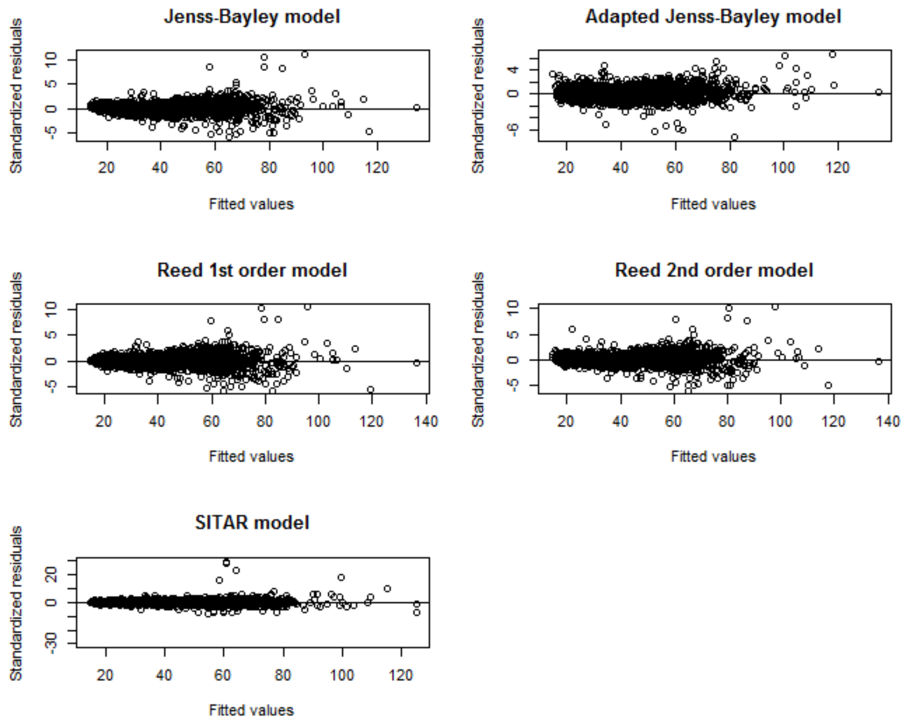

Figure 3.2: Females' scatter plots of standardized residuals against fitted values from the fitted models

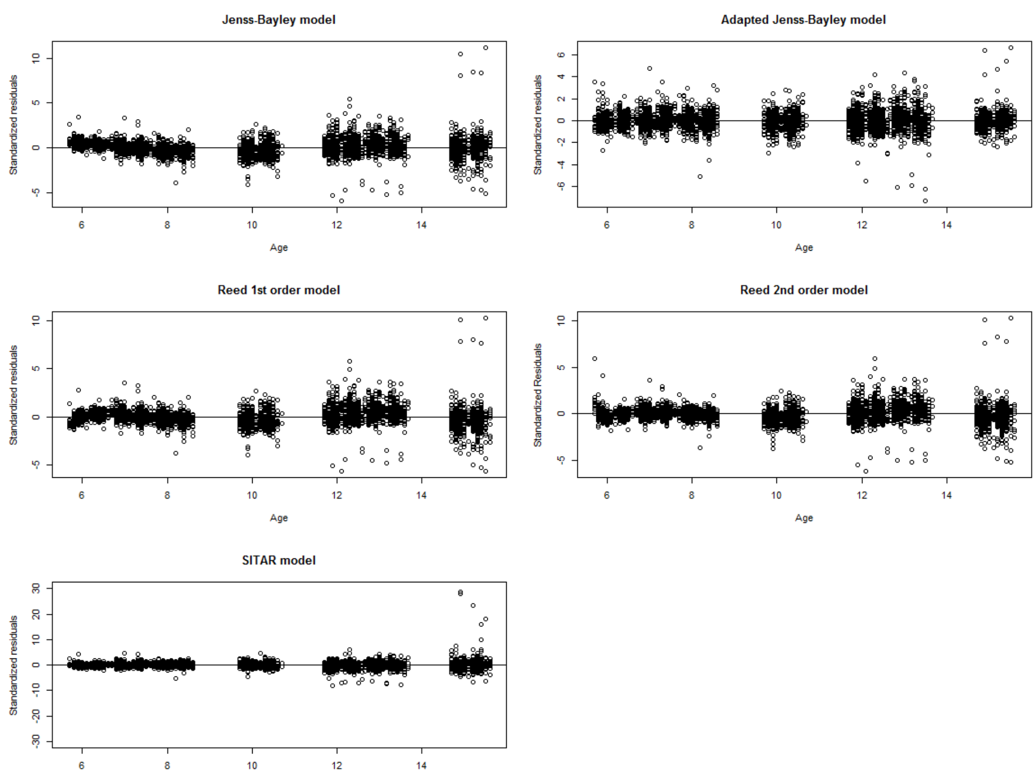

Figure 3.3: Females' scatter plots of standardized residuals against age from the fitted models

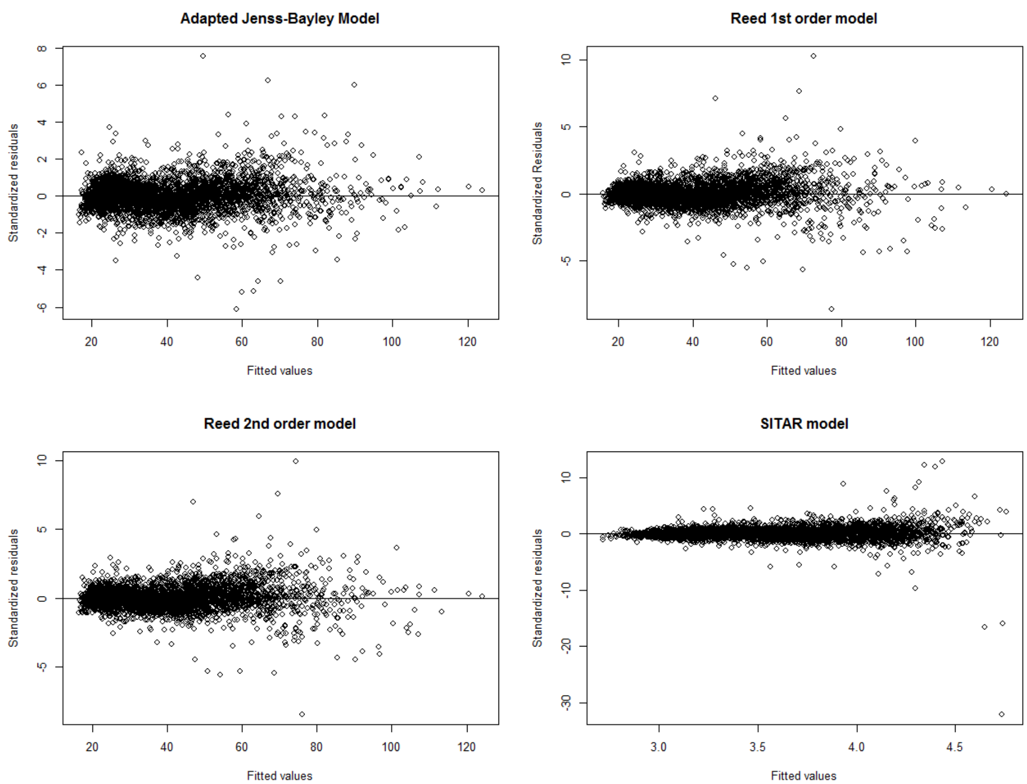

Figure 3.4: Males' scatter plots of standardized residuals against fitted values from the fitted models

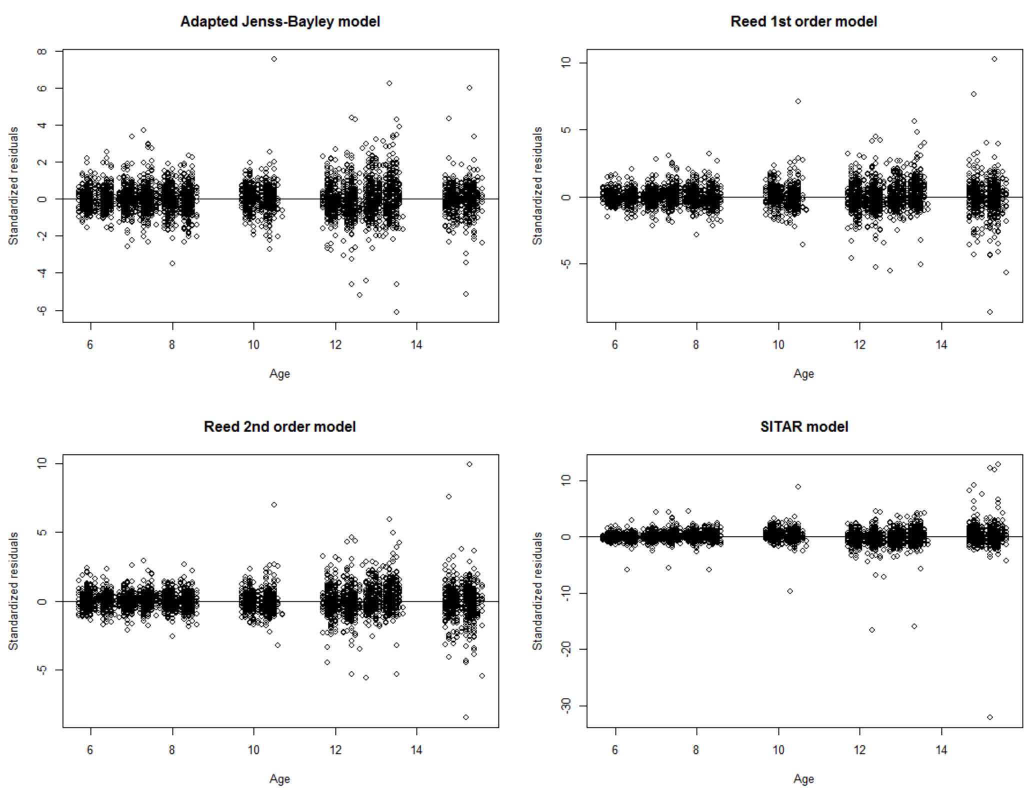

Figure 3.5: Males' scatter plots of standardized residuals against age from the fitted models

The normal probability plots of the standardized residuals for females (Figure 3.6) and males (Figure 3.7) showed that the assumption of normality of the errors was best satisfied by the SITAR model in both the sexes as compared to the other growth models. The normal probability plots from the SITAR models shows that the standardized residuals had a moderate departure from the reference fitted line at both the lower and upper ends of the line. This indicated that the SITAR models standardized residuals were approximately normally distributed with heavy tails at the ends and have few outlying observations. The normality assumption was violated by other growth models as the normal probability plots showed serious departures from the fitted line at both the ends except for females Adapted Jenss-Bayley model that showed a slight departure from the line particularly at the left end.

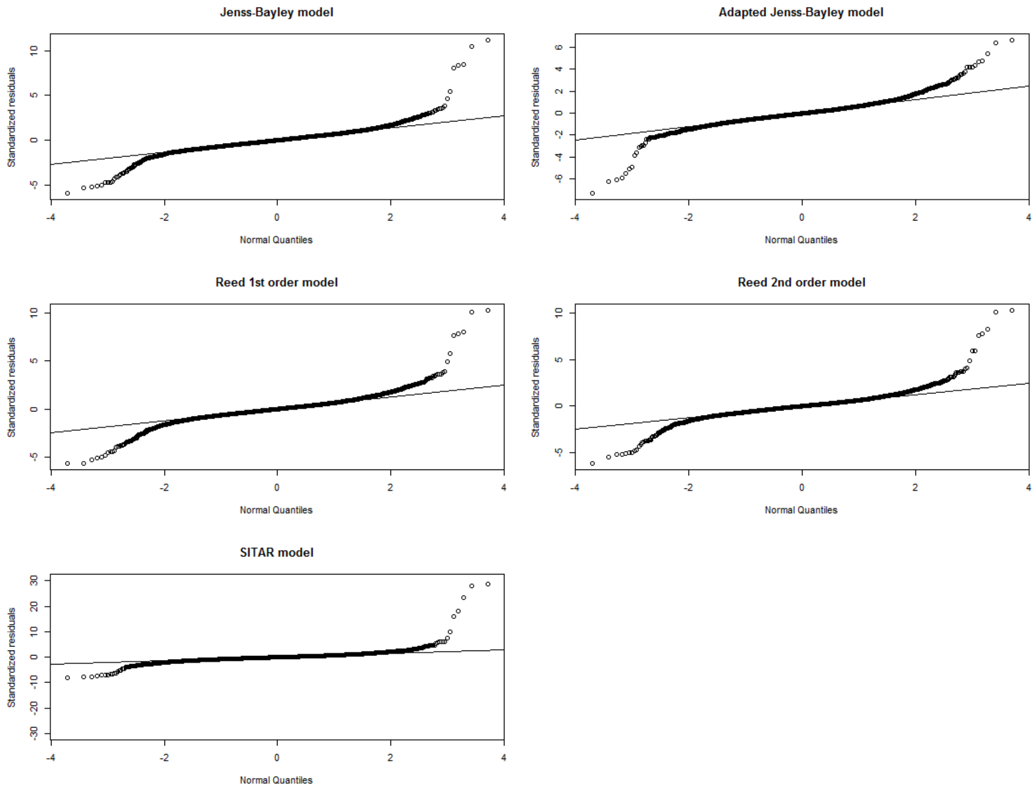

Figure 3.6: Females' normal probability plots from the fitted models

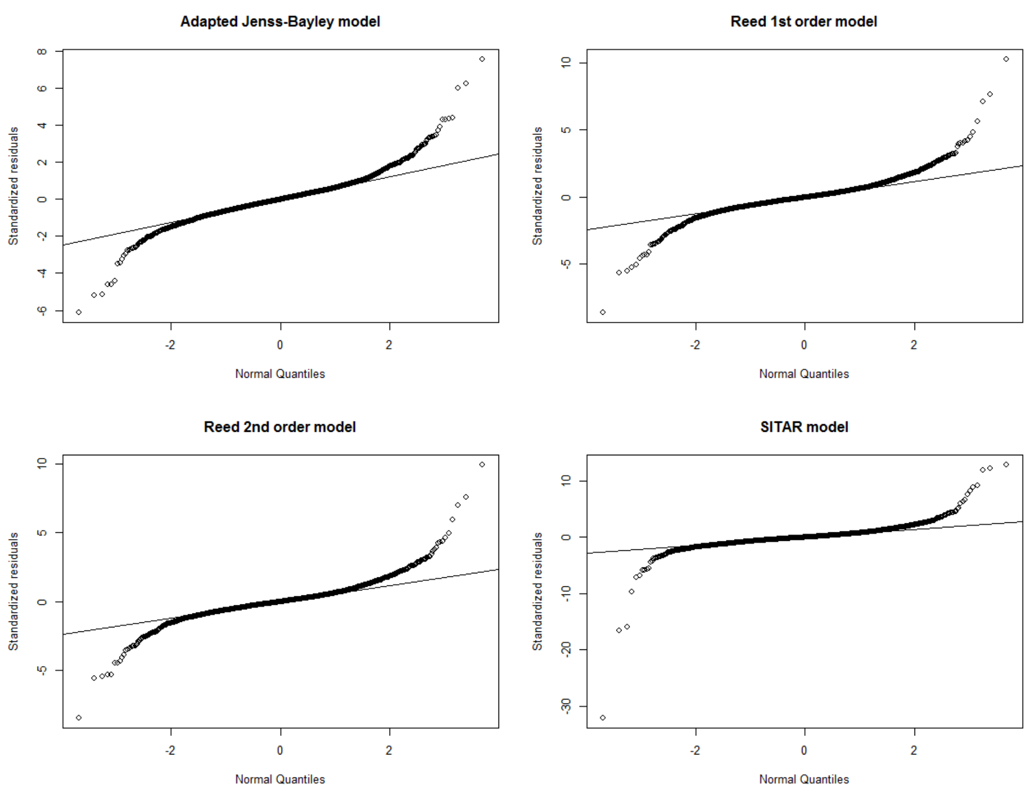

Figure 3.7: Males' normal probability plots from the fitted models

3.4 Summary and comparison of models

The results from the different specification of the SITAR model that fitted best for both females and males is the untransformed age and the natural logarithm of weight model when size and tempo were fitted as fixed effects and size, tempo and velocity as random effects. The log transformation of weight for four models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order and Adapted Jenss-Bayley) was also considered in order to be consistent with the best fitted SITAR models. Thus, to determine the best model within each theory, the untransformed weight model was compared with the log transformed weight model for the four theories. The results are shown in Table 3.7 for both females and males. The untransformed and log transformed weight models within each theory are non-nested models, with AIC, BIC and RSD values. The four models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley) were compared separately for females and males. From the Table 3.7, it was observed that for both females and males, the log transformed weight model within each theory performed better than the untransformed weight model.

Table 3.7: Comparison of non-nested models within each theory for females and males

	Females			**Males**		
Model	**RSD**	**AIC**	**BIC**	**RSD**	**AIC**	**BIC**
Jenss-Bayley						
Weight	3.73	29427.35	29479.15	Failed to converge		
Log(weight)	2.54	26405.14	26456.94	2.49	24040.68	24091.66
Adapted Jenss-Bayley						
Weight	2.56	27723.8	27801.5	2.53	25134.27	25210.7
Log(weight)	2.02	25544.44	25622.14	2.04	23478.28	23554.76
Reed 1^{st} order						
Weight	3.8	29525.78	29577.59	3.17	25781.72	25832.7
Log(weight)	2.81	27043.94	27095.74	2.52	24092.58	24143.56
Reed 2^{nd} order						
Weight	3.62	29279.16	29356.87	3.09	25700.75	25777.2
Log(weight)	2.57	26573.84	26651.54	2.48	24008.71	24085.18

RSD: Residual Standard Deviation, AIC: Akaike Information Criteria
BIC: Bayesian Information Criteria

Upon the identification of the best fitted model within each theory (from Table 3.7), Tables 3.8 and 3.9 explores the comparison of the best fitted models across all theories with one another. The best fitted models in Tables 3.8 and 3.9 will be highlighted in bold. The log weight transformed Adapted Jenss-Bayley model is an extension of the log weight transformed original Jenss-Bayley model that includes an extra quadratic term. Therefore, these are nested models and were compared using the Log likelihood ratio test. The p-value <.0001 indicated that the log weight transformed Adapted Jenss-Bayley model was considered to be a better fit than the log weight transformed Jenss-Bayley model. The log weight transformed Reed 2^{nd} order model is also an extension of log weight transformed Reed 1^{st} order including an inverse of age square term indicating that log weight transformed Reed 1^{st} order model is nested within Reed 2^{nd} order model. The p-value <.0001 obtained using the Log likelihood ratio test indicated that log weight transformed Reed 2^{nd} order performed better than log weight transformed Reed 1^{st} order. The log weight transformed Adapted Jenss-Bayley, Reed 2^{nd} order and SITAR models are non-nested models and thus were compared in terms of AIC and BIC criteria. The fit statistics indicated that the SITAR models outperformed all models for both females and males.

Table 3.8: Comparison of the goodness of fit of the five fitted models for females on the log transformed weight scale

Model	**RSD**	**AIC**	**BIC**	**Log-Likelihood**	**Likelihood-Ratio**	**p-value**
Jenss-Bayley	2.54	26405.14	26456.94	-13194.57		
Adapted Jenss-Bayley	2.02	25544.44	25622.14	-12760.22	868.7	<.0001
Reed 1^{st} order	2.81	27043.94	27095.74	-13513.97		
Reed 2^{nd} order	2.57	26573.84	26651.54	-13274.92	478.12	<.0001
SITAR	**1.96**	**25307.99**	**25385.69**	**-12641.99**		

RSD: Residual Standard Deviation, AIC: Akaike Information Criteria
BIC: Bayesian Information Criteria

Table 3.9: Comparison of the goodness of fit of the five fitted models for males on the log transformed weight scale

Model	**RSD**	**AIC**	**BIC**	**Log-Likelihood**	**Likelihood-Ratio**	**p-value**
Jenss-Bayley	2.49	24040.68	24091.66	-12012.36		
Adapted Jenss-Bayley	2.04	23478.28	23554.76	-11727.16	570.396	<.0001
Reed 1^{st} order	2.52	24092.58	24143.56	-12038.29		
Reed 2^{nd} order	2.48	24008.71	24085.18	-11992.36	91.86	<.0001
SITAR	**2.14**	**23382.68**	**23459.16**	**-11679.34**		

RSD: Residual Standard Deviation, AIC: Akaike Information Criteria
BIC: Bayesian Information Criteria

Tables 3.10 and 3.11 explores the comparison of the untransformed weight models (Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} order, and Reed 2^{nd} order) with the best model (SITAR) selected from Tables 3.8 and 3.9 for females and males respectively. The best models in Tables 3.10 and

3.11 will be highlighted in bold. The results (from Tables 3.10 and 3.11) were not affected when the untransformed weight Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models were compared with the best fitted SITAR model for both females and males. It was observed that SITAR continued to be the best fitted weight growth model from middle childhood to adolescence based on lowest AIC, BIC and RSD values. Thus, for the ease of interpretation, the parameter estimates and plots were interpreted from the untransformed Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models alongside the SITAR model.

Table 3.10: Comparison of the untransformed weight models (Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order) with the SITAR model for females

Model	**RSD**	**AIC**	**BIC**	**Log-Likelihood**	**Likelihood-Ratio**	**p-value**
Jenss-Bayley	3.73	29427.35	29479.15	-14705.67		
Adapted Jenss-Bayley	2.56	27723.8	27801.5	-13849.9	1711.55	<.0001
Reed 1^{st} order	3.8	29525.78	29577.59	-14754.89		
Reed 2^{nd} order	3.62	29279.16	29356.87	-14627.58	254.62	<.0001
SITAR	2.02	25307.99	25385.69	-12641.99		

RSD: Residual Standard Deviation, AIC: Akaike Information Criteria
BIC: Bayesian Information Criteria

Table 3.11: Comparison of the untransformed weight models (Jenss-Bayley, Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order) with the SITAR model for males

Model	**RSD**	**AIC**	**BIC**	**Log-Likelihood**	**Likelihood-Ratio**	**p-value**
Jenss-Bayley	-	-	-	-		
Adapted Jenss-Bayley	2.53	25134.27	25210.7	-12555.13		
Reed 1^{st} order	3.17	25781.72	25832.7	-12881.65		
Reed 2^{nd} order	3.09	25700.75	25777.2	-12838.38	86.54	<.0001
SITAR	2.14	23382.68	23459.2	-11679.34		

RSD: Residual Standard Deviation, AIC: Akaike Information Criteria
BIC: Bayesian Information Criteria

3.5 Population level predicted growth curves

The population level predicted weight growth curves of females [in red] and males [in blue] from the best fitted Adapted Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order and SITAR models were superimposed on the average trajectory over time as shown in Figure 3.8. The best specification of the SITAR models was fitted on the log weight and age scale, thus the curves predicted by these models have been back transformed so that the predicted weights were on the same scale for all the models. The population level predicted curves for females and males of Jenss-Bayley model are not shown because the model failed on the males' data.

As previously stated, the Reed 1^{st} and 2^{nd} order models performed worse than Adapted Jenss-Bayley and SITAR models for both females and males. Consistent with this finding, Figure 3.8 demonstrated that the population level predicted growth curves of Reed (1^{st} and 2^{nd}) order models did not fit well for females' data at the start of the curve. These predicted curves for Reed 1^{st} and 2^{nd} order models curves provided more or less a linear fit but a closer fit or exact fit (at some time points) to the observed average weight trajectory over time for both females and males. In contrast, Adapted Jenss-Bayley and SITAR models predicted curves demonstrates an "S" shaped pattern of children's growth from middle childhood to adolescence. The Figure 3.8 depicted that the end part of the males' curve of Adapted Jenss-Bayley suggests that males are reaching their final body weight. This is inaccurate as the observed weight growth curves suggests that the males are not done growing. In contrast, SITAR model captures the end part of the curve, and accurately depicts males weight as still increasing. Also, based on AIC, BIC and RSD values, the SITAR model performed better than Adapted Jenss-Bayley. The SITAR model also has an advantage over other models that it provides biological interpretation of its parameters.

The predicted curves from the SITAR model (Figure 3.8) shows that the growth of females and males is constant and parallel to each other until the age of 8.5 years approximately. During this period of time the males' predicted curve lies above the females' curve indicating that males' were slightly heavier than females'. There was no difference in the predicted curves for females and males as they overlap to each other for about 1 year i.e. until 9.5 years of age approximately. The females' growth then started diverging from the males' at around 9.5 years of age and they began gaining weight more rapidly than males. Females' continue to gain weight and tend to be heavier than males' until 14 years approximately. On the other hand, around age 14 when females' were growing more slowly than before, the males' started gaining more weight than females and they tend to be heavier than females' until 16 years of age.

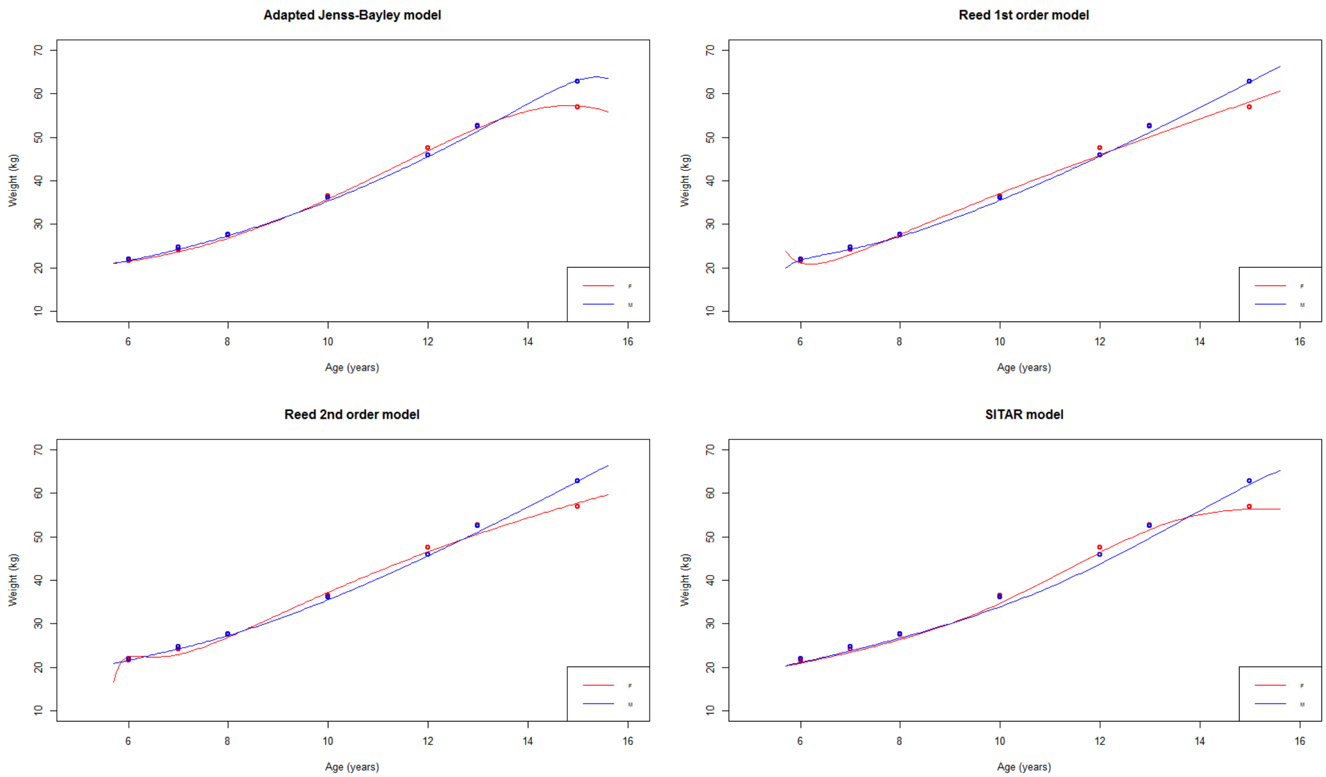

Figure 3.8: Population predicted level weight growth curves of females and males from the fitted growth models superimposed on the observed average weight values represented by (o)

The population velocity curve for females (Figure 3.9) obtained from the SITAR model demonstrates that they have a linear rate of growth until 8 years of age. This was then followed by a rapid increase in velocity indicating that the females will enter in their pubertal growth spurt phase earlier than males. Females' pubertal spurt continues until it reaches APWV of 11.43 years with PV of 5.99 kg per year and then the velocity starts decelerating rapidly after reaching APWV. On the other hand, males' experience linear velocity until 10 years of age followed by a sudden increase in velocity having PWV of 6.29 kg per year at the age of 13.66 years where males reach APWV approximately 2 years after females reaches their APWV.

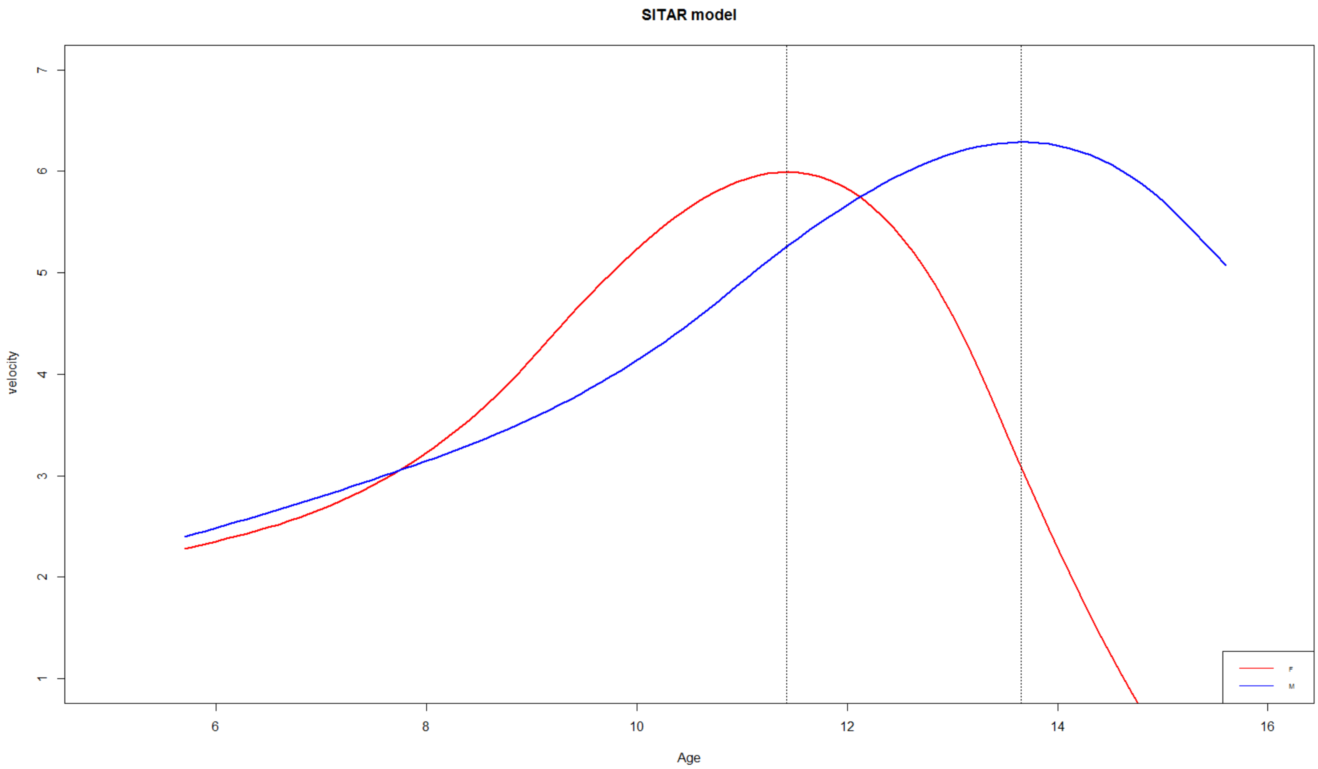

Figure 3.9: Weight velocity curves from the best fitted SITAR models for females and males

Tables 3.12 and 3.13 compares the weight predicted by the five models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, Adapted Jenss-Bayley, and SITAR) with observed weight at selected ages for females and males respectively. For females', the overall results from Table 3.14 showed that the Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models predicted the weight very closely to the observed weight at ages 6, 10 and 15 except at age 6 for Jenss-Bayley and at age 15 for Reed 2^{nd} order. The Adapted Jenss-Bayley model also predicted weight closely to the observed weight whereas SITAR model predicted weight approximate to the observed weight at each age. On the other hand, for males (Table 3.15), the Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models also predicted weight very closely to the observed weight than the SITAR model.

Table 3.12: Average predicted weight from five fitted models for females at selected ages

		Predicted Weight(kg)				
Ages	**Oberved weight(kg)**	**JB**	**AJB**	**R1**	**R2**	**SITAR**
6	21.68	19.07	21.55	21.13	22.44	20.71
10	36.46	37.35	35.83	37.1	37.23	34.66
15	56.85	57.39	55.93	58.15	57.75	56.37

JB: Jenss-Bayley, AJB: Adapted Jenss-Bayley, R1: Reed 1^{st} order, R2: Reed 2^{nd} order

Table 3.13: Average predicted weight from five fitted models for males at selected ages

		Predicted Weight(kg)				
Ages	**Observed weight(kg)**	**JB**	**AJB**	**R1**	**R2**	**SITAR**
6	22	-	21.66	21.66	21.61	21.44
10	36.23	-	35.37	35.05	35.55	33.83
15	62.86	-	63.14	62.83	62.78	62.37

JB: Jenss-Bayley, AJB: Adapted Jenss-Bayley, R1: Reed 1^{st} order, R2: Reed 2^{nd} order

Chapter 4

Discussion and conclusion

This research study included an analytic sample of 1737 children from Quebec, Canada whose body weight was measured from 6 to 15 years of age. This study focused on comparing the performance of different anthropometric growth models on the weight measurements of the subjects. Five anthropometric models (Jenss-Bayley and Reed models and their extensions alongside a newly developed SITAR model) were examined. This paper used a mixed effects approach to compare these models and showed the strengths and limitations of each model. The difficulties encountered in fitting each of these models under this framework were also discussed. The Jenss-Bayley, Reed 1^{st} order and Reed 2^{nd} order models have been originally conceptualized to be applied to model growth between birth to 6 years (Jenss & Bayley, 1937; Berkey & Reed, 1987) and some previous studies have applied these models between birth to 10 years of age (Chirwa, Griffiths, Maleta, Norris, & Cameron, 2014; Regnault, Gillman, Kleinman, Rifas-Shiman, & Botton, 2014). To date, no previous study has compared these models across an age range that does not necessarily start at birth and includes puberty under a mixed effect framework.

The mixed effect approach accounts for average growth patterns of the general population as well as an individual's variation around that average growth. Using this approach, each child's growth curve can be modelled simultaneously by defining an overall model for the children. Before the mixed effect approach came into the literature of longitudinal analysis, the anthropometric models were used to fit just an average growth curve of the sample. In addition, these previous models were used to fit each child separately to predict an individual's growth curve. Unlike historical approaches of longitudinal data analysis which required balanced designs, the mixed effect approach is more flexible and can handle unbalanced study designs.

The models were fitted using the nlme function in R and required good starting values for their growth parameters to avoid convergence problems. In general, non-linear models in comparison to the linear models are not easy to fit as the former requires good initial values for the estimation of their growth parameters. Reed models are linear models and could be fitted using the lme (linear mixed effect) function in R but in order to be consistent with the other models, they were fitted using the nlme function in R. No differences were observed in the parameters estimates and their standard errors when Reed models were fitted with lme and nlme functions in R.

The findings from this research showed that the four parameter Jenss-Bayley and Reed 1^{st} order models failed to converge when all the random effects of the growth parameters were added. They only converged when the random effects of the intercept and the slope were added to the models but the Jenss-Bayley model continued to fail when fitted on the males data. This may imply that the model may be over parameterized for the males' data in the age range (6-15 years) and does not require the exponent term in the model. However, this suggests that the males' follow constant growth for a longer period of time than females and also their pubertal spurt starts later than them perhaps at the age of 13 or 14 years (at the end of the curve). Some males may start their puberty at the same time as other males which affects their weight and some starts it later that could have led to strong computational problems for the model convergence. In addition, the Jenss-Bayley model fails to capture the end part of the growth spurt when the weight velocity starts decreasing for the males' data. The Adapted Jenss-Bayley and Reed 2^{nd} order converged when the random effects of the intercept, as well as when slope were added. The random effects of their fifth parameter were also added.

All the parametric models (Jenss-Bayley and Reed models and their extensions) conclude that there are variations in individuals' intercepts and growth curve slopes. The Adapted Jenss-Bayley's random effect of the velocity that is captured at the onset of the puberty is indicative of the fact that the velocities of the children differ from one another when the adolescent spurt starts and experiences either faster or slower velocities than the average. The Reed 1^{st} order and Reed 2^{nd}

order for females did not provide valid and logical estimates of the growth parameters whereas the estimates for the males from the same models provided far better estimates than females. All four models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley) did not converge when the random effects of the deceleration parameters were added. This non-convergence could have been due to the fact that the children follow constant growth during childhood and thus not much deceleration in growth takes place during this phase. In addition, it can be concluded that no variations are observed across individuals when the decrease in velocity takes place after the pubertal growth spurt.

The newly developed SITAR model was first fitted with all fixed and random effects of the parameters where spline function was fitted as a fixed effect. Some non-convergence issues were observed when the SITAR parameters were fitted both as fixed and random. Thus, alternative restrictions on the fixed effects were imposed in order to achieve convergence. Due to the limited number of measurement occasions available, only 3 degrees of freedom were selected to fit the spline curve.

It was concluded that the SITAR model outperformed the other four models (Jenss-Bayley, Reed 1^{st} order, Reed 2^{nd} order, and Adapted Jenss-Bayley) and was the best fitted growth model which modeled weight well during middle childhood and adolescence (from 6 to 15 years). The SITAR models were also fitted with different degrees of freedom (2, 4 and 5) and were compared with other growth models. It was observed that the SITAR model performed better than the other four models. The SD's of the random effects of the models (Jenss-Bayley, Reed 1^{st} and 2^{nd} order, Adapted Jenss-Bayley) were significantly higher than the SITAR model. In addition, the population level predicted growth curves of the former models provided a more closer fit to the observed weight trajectory than the SITAR model. However, it was observed that the Reed 1^{st} and 2^{nd} order models provided the worst fit based on the fit statistics and Adapted Jenss-Bayley performed the second best than the SITAR model. This is in contrast to the finding of a previous study by Pizzi et al. (2014) which showed that the Reed 1^{st} order model performed the best compared to the SITAR model based on the fit statistics.

The Adapted Jenss-Bayley provided a better fit than Reed 1^{st} and 2^{nd} order models in terms of minimum AIC and BIC values. Previous work done by Regnault et al. (2014) compared Jenss-

Bayley, Adapted Jenss-Bayley, Reed 1^{st} and Reed 2^{nd} order models in US children to model weight from birth to late childhood (up to 9 years) and showed that Adapted Jenss-Bayley fitted the best. This study extended the findings of Regnault et al. (2014) to confirm that the model continued to fit well into adolescence phase (up to 15 years) even when the weight growth was modelled from 6 years rather than from birth.

The present study concluded that Reed 1^{st} order provided the worst fit to both females and males data during the middle childhood to adolescence phase. Results are inconsistent with previous studies by Pizzi et al. (2014), Berkey (1987), and Chirwa et al. (2014) which showed that Reed 1^{st} order model performed the best from birth until late childhood (10 years) even compared to SITAR. This is possibly due to the age range that had been analyzed in this present study as it was starting from 6 years, rather than starting at birth. In particular, as the Reed 1^{st} order model was originally suggested to describe growth from early life months to middle childhood, the appropriateness of this model for later childhood is questionable. Indeed from the population level predicted curves of the models, it was concluded that the Reed models did not provide a good fit as they showed systematic deficiencies between the ages of 6 and 7 for females. In general, the growth pattern of children follows an "S" shaped pattern and this shape was much closer captured by Adapted Jenss-Bayley and SITAR models whereas Reed models provided more of a linear fit to the data.

In general, the Reed 1^{st} order and Reed 2^{nd} order models can identify one and two inflection points respectively but, in this study, they failed to identify the peaks. APWV also cannot be achieved by the Jenss-Bayley model because the growth function's second derivative with respect to t is an exponential function in t and hence does not allow for any inflection point in the curve (Pizzi et al., 2014). The APWV could be achieved with the Adapted Jenss-Bayley model as its second derivative is not an exponential function in t. But this model failed to identify the peak even when it is actually present. Among the five models, only SITAR model was able to identify the peak in its velocity curve and thus allowed the identification of an age when the weight velocity was maximum. Therefore, from the SITAR model it was concluded that females have APWV of 11.43 years with PWV of approximately 6 kg per year whereas males have APWV of 13.66 years with PWV of 6.29 kg per year.

This study has some limitations. Firstly, a limited number of weight measurements occasions (7) were available over a larger period of 10 years. These measurements were quite far apart from each other as they were collected annually from 6 to 8 years and then bi-annually from 8 to 15 years. This led to the loss of information on the change in weight between these years. Having more measurements available for the children would have helped in improving the fit of all the models. Secondly, the weight data were unbalanced as the weight measurements were not collected at fixed time points for all the individuals and also due to lost to follow-up. Although children with at least one measurement were included in the analysis, the average number of measures was 5, and approximately 40% of the sample had all seven measurements. Thirdly, as data collection is ongoing and the participants are just now reaching adulthood, data at the end of the adolescence phase is not yet available. Fourthly, an independent covariance structure was assumed for within subject errors in accordance with the previous studies. Different covariance structures should be explored in the future studies. The study should be reassessed when the children reach 18 years of age (i.e. when the growth has stopped). Future research should incorporate other parameter(s) in Adapted Jenss-Bayley so that it could model the growth starting from birth to post puberty. The future studies should also consider other transformations for the weight variable other than the log transformation. All the models explored in this study should be compared in smaller data range (after puberty or before puberty). Lastly, the cross-validation was not conducted as it was beyond the scope of this study and should be considered for the future work.

Body weight is a very sensitive growth measurement which is more directly affected by illness or loss of appetite than any other growth measurement. In addition, various negative environmental factors play a major role that affects children's weight. In recent decades, an abnormal increase in the weight of children has become a major health concern worldwide. Thus, the models present in this study should also be applied and compared while describing BMI trajectories of children from middle childhood to adolescence age which has not been explored in this study. This research study has discussed and addressed the difficulties of fitting traditional parametric models and the newly developed SITAR model to an age range starting from middle childhood to adolescence. The advantages and disadvantages of each model have been discussed in detail. Out of all the models that were presented in this paper, the SITAR model overall performed the best for this study. The

SITAR model is very flexible because of its ability to fit the data of any age range and can be applied to any anthropometric growth measurement. Another significance of using the SITAR model over others is that it allows identification of APWV and PWV and has direct biological interpretation of its parameters. The derived parameters from this model can be used in further research as the predictors for various health outcomes in adult life. While the SITAR model is the best performing model in this study, the comparison of the models should be reassessed in additional studies with longer follow up.

References

Akaike, H. (1978). On the likelihood of a time series model. *The Statistician*, 217-235.

Asefa, M., Drewett, R., & Hewison, J. (1996). An ethiopian birth cohort study. *Paediatric and perinatal epidemiology*, *10*(4), 443-462.

Balaban, N. E., & Bobick, J. E. (2008). *The handy anatomy answer book*. Visible Ink Press.

Barker, D. J. (2004). The developmental origins of chronic adult disease. *Acta Paediatrica*, *93*(s446), 26-33.

Barker, D. J. (2012, Mar). Sir richard doll lecture. developmental origins of chronic disease. *Public health*, *126*(3), 185-189. (LR: 20120314; CI: Copyright A(c) 2011; JID: 0376507; 2011/11/30 00:00 [accepted]; 2012/02/14 06:00 [entrez]; 2012/02/14 06:00 [pubmed]; 2012/05/26 06:00 [medline]; ppublish) doi: 10.1016/j.puhe.2011.11.014[doi]

Barker, D. J., Osmond, C., Winter, P., Margetts, B., & Simmonds, S. J. (1989). Weight in infancy and death from ischaemic heart disease. *The Lancet*, *334*(8663), 577-580.

Barnes, H. V. (1975). Physical growth and development during puberty. *Medical Clinics of North America*, *59*(6), 1305-1317.

Beath, K. J. (2007). Infant growth modelling using a shape invariant model with random effects. *Statistics in medicine*, *26*(12), 2547-2564.

Beath, K. J. (2012). Infant growth modelling and assessment of growth. In (p. 3045-3056). Springer.

Berkey, C. S. (1982). Comparison of two longitudinal growth models for preschool children. *Biometrics*, 221-234.

Berkey, C. S., & Reed, R. B. (1987). A model for describing normal and abnormal growth in early childhood. *Human biology*, 973-987.

Bock, R. D., & Thissen, D. (1976). Fitting multi-component models for growth in stature. In

Proceedings of the 9th international biometric conference (Vol. 1, p. 431-442).

Bogin, B. (2015). Human growth and development. In (p. 285-293). Elsevier.

Botton, J., Heude, B., Maccario, J., Ducimetiere, P., Charles, M. A., & Group, F. S. (2008, Jun). Postnatal weight and height growth velocities at different ages between birth and 5 y and body composition in adolescent boys and girls. *The American Journal of Clinical Nutrition*, *87*(6), 1760-1768. (LR: 20170220; JID: 0376027; CIN: Am J Clin Nutr. 2008 Jun;87(6):1587-9. PMID: 18541543; OID: NLM: PMC4767885; ppublish) doi: 87/6/1760[pii]

Box, G. E., & Cox, D. R. (1964). An analysis of transformations. *Journal of the Royal Statistical Society.Series B (Methodological)*, 211-252.

Cameron, N. (2007). Growth patterns in adverse environments. *American Journal of Human Biology*, *19*(5), 615-621.

Cameron, N., & Bogin, B. (2012). *Human growth and development*. Academic Press.

Chirwa, E. D., Griffiths, P. L., Maleta, K., Norris, S. A., & Cameron, N. (2014). Multi-level modelling of longitudinal child growth data from the birth-to-twenty cohort: a comparison of growth models. *Annals of Human Biology*, *41*(2), 168-179.

Cole, & Cole, M. T. (2017). Package 'sitar'.

Cole, Donaldson, M. D., & Ben-Shlomo, Y. (2010). Sitar—a useful instrument for growth curve analysis. *International journal of epidemiology*, *39*(6), 1558-1566.

Cole, Kuh, D., Johnson, W., Ward, K., Howe, L. D., Adams, J. E., ... Ong, K. (2016). Using super-imposition by translation and rotation (sitar) to relate pubertal growth to bone health in later life: the medical research council (mrc) national survey of health and development. *International journal of epidemiology*, *45*(4), 1125-1134.

Cole, & Mori, H. (2018). Fifty years of child height and weight in japan and south korea: Contrasting secular trend patterns analyzed by sitar. *American Journal of Human Biology*, *30*(1), e23054.

Count, E. W. (1943). Growth patterns of the human physique: an approach to kinetic anthropometry: Part i. *Human Biology*, *15*(1), 1-32.

Curran, P. J., Obeidat, K., & Losardo, D. (2010, 04/30). Twelve frequently asked questions about growth curve modeling. *Journal of Cognition and Development*, *11*(2), 121-136. Retrieved from `http://dx.doi.org/10.1080/15248371003699969` (doi: 10.1080/15248371003699969) doi: 10.1080/15248371003699969

Deming, J., & Washburn, A. H. (1963). Application of the jenss curve to the observed pattern of growth during the first eight years of life in forty boys and forty girls. *Human biology*, *35*(4), 484-506.

de Waal, H. A. D.-V. (1993, Jul). Environmental factors influencing growth and pubertal development. *Environmental health perspectives*, *101 Suppl 2*, 39-44. (LR: 20130919; JID: 0330411; 1993/07/01 00:00 [pubmed]; 1993/07/01 00:01 [medline]; 1993/07/01 00:00 [entrez]; ppublish)

Dwyer, J. T., Andrew, E. M., Berkey, C., Valadian, I., & Reed, R. B. (1983, May). Growth in "new" vegetarian preschool children using the jenss-bayley curve fitting technique. *The American Journal of Clinical Nutrition*, *37*(5), 815-827. (LR: 20091119; GR: HD08958/HD/NICHD NIH HHS/United States; GR: K04 AM00272/AM/NIADDK NIH HHS/United States; JID: 0376027; ppublish)

Ellis, R. W. B. (1951). Phases of postnatal growth. *British Journal of Nutrition*, *5*(1), 151-157. doi: 10.1079/BJN19510018

Fitzmaurice, G. M., Laird, N. M., & Ware, J. H. (2012). *Applied longitudinal analysis* (Vol. 998). John Wiley and Sons.

Ge, X., Brody, G. H., Conger, R. D., Simons, R. L., & Murry, V. M. (2002). Contextual amplification of pubertal transition effects on deviant peer affiliation and externalizing behavior among african american children. *Developmental psychology*, *38*(1), 42.

Haralabakis, N. B., & Spyropoulou, M. N. (1990, Jun). Factors affecting human growth. *Odontostomatologike proodos*, *44*(3), 167-177. (LR: 20061115; JID: 0401104; 0 (Gonadal Steroid Hormones); 0 (Thyroid Hormones); 9002-72-6 (Growth Hormone); RF: 44; ppublish)

Hauspie, R., Cameron, N., Molinari, L., & MyiLibrary. (2004). *Methods in human growth research* (Vol. 39). Cambridge, UK; New York: Cambridge University Press. ([electronic resource] / edited by Roland C. Hauspie, Noël Cameron, Luciano Molinari.; online resource;) :ill; Title from e-book title screen (viewed October 17, 2007); Includes bibliographical references and index.; Electronic reproduction.UK :MyiLibrary,2007 Available via World Wide Web.Access may be limited to MIL affiliated libraries.; Cambridge University Press e-books (CRKN DCI Project); Cambridge studies in biological and evolutionary anthropology ;39.)

Hauspie, R., & Roelants, M. (2013). Adolescent growth. In (p. 57-79). Elsevier.

Hui, L., Leung, G. M., Cowling, B. J., Lam, T., & Schooling, C. M. (2010). Determinants of infant growth: evidence from hong kong's "children of 1997" birth cohort. *Annals of Epidemiology*, *20*(11), 827-835.

Jenss, R. M., & Bayley, N. (1937). A mathematical method for studying the growth of a child. *Human Biology*, *9*(4), 556.

Jetté, M. (2002). Quebec longitudinal study of child development (qlscd 1998-2000, vol. 2, no. 1). survey description and methodology (part i: Logistics and longitudinal data collections). *Québec, Canada: Institut de la statistique du Québec.*.

Jetté, M., & Groseillers, L. D. (2000). Survey description and methodology québec longitudinal study of child development (qlscd 1998–2002), volume 1, number 1. *Québec: Institut de la statistique du Québec*.

Johnson, L., Llewellyn, C. H., Jaarsveld, C. H. V., Cole, T. J., & Wardle, J. (2011). Genetic and environmental influences on infant growth: prospective analysis of the gemini twin birth cohort. *PloS one*, *6*(5), e19918.

Jolicoeur, P., Pontier, J., Pernin, M.-O., & Sempé, M. (1988). A lifetime asymptotic growth curve for human height. *Biometrics*, 995-1003.

Karlberg, J. (1987). On the modelling of human growth. *Statistics in medicine*, *6*(2), 185-192.

Karlberg, J. (1990). The infancy–childhood growth spurt. *Acta Paediatrica*, *79*(s367), 111-118.

Largo, R., Gasser, T., Prader, A., Stuetzle, W., & Huber, P. (1978). Analysis of the adolescent growth spurt using smoothing spline functions. *Annals of Human Biology*, *5*(5), 421-434.

Lawton, W., Sylvestre, E., & Maggio, M. (1972). Self modeling nonlinear regression. *Technometrics*, *14*(3), 513-532.

Malina, R. M. (2012). Growth. In (p. 376-378). Springer.

Manwani, A., & Agarwal, K. (1973). The growth pattern of indian infants during the first year of life. *Human biology*, 341-349.

Marceau, K., Ram, N., Houts, R. M., Grimm, K. J., & Susman, E. J. (2011). Individual differences in boys' and girls' timing and tempo of puberty: Modeling development with nonlinear growth models. *Developmental psychology*, *47*(5), 1389.

Mathieu, M. E., Drapeau, V., & Tremblay, A. (2010). Parental misperception of their child's body weight status impedes the assessment of the child's lifestyle behaviors. *International journal of pediatrics*, *2010*, 10.1155/2010/306703. Epub 2010 Sep 2. (LR: 20170220; JID:

101517077; 2010/01/14 00:00 [received]; 2010/07/13 00:00 [accepted]; 2010/09/24 06:00 [entrez]; 2010/09/24 06:00 [pubmed]; 2010/09/24 06:01 [medline]; ppublish) doi: 10.1155/2010/306703[doi]

Pan, H., & Goldstein, H. (1998). Multi-level repeated measures growth modelling using extended spline functions. *Statistics in medicine*, *17*(23), 2755-2770.

Patton, G. C., & Viner, R. (2007). Pubertal transitions in health. *The Lancet*, *369*(9567), 1130-1139.

Pinheiro, Bates, D., DebRoy, S., Sarkar, D., Heisterkamp, S., Willigen, B. V., & Maintainer, R. (2017). Package 'nlme'. *Linear and nonlinear mixed effects models*, 3-1.

Pinheiro, & Bates, D. M. (2000). Mixed-effects models in s and s-plus springer. *New York*.

Pizzi, C., Cole, T. J., Corvalan, C., dos Santos Silva, I., Richiardi, L., & Stavola, B. L. D. (2014). On modelling early life weight trajectories. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, *177*(2), 371-396.

Preece, M., & Baines, M. (1978). A new family of mathematical models describing the human growth curve. *Annals of Human Biology*, *5*(1), 1-24.

Regnault, N., Gillman, M. W., Kleinman, K., Rifas-Shiman, S., & Botton, J. (2014). Comparative study of four growth models applied to weight and height growth data in a cohort of us children from birth to 9 years. , *65*(2-3), 167-174. doi: 10.1159/000365894[doi]

Riddell, C. A., Platt, R. W., Bodnar, L. M., & Hutcheon, J. A. (2017). Classifying gestational weight gain trajectories using the sitar growth model. *Paediatric and perinatal epidemiology*, *31*(2), 116-125.

Rodd, C., Metzger, D. L., & Sharma, A. (2014). Extending world health organization weight-for-age reference curves to older children. *BMC pediatrics*, *14*(1), 32.

Sakamoto, Y., Ishiguro, M., & Kitagawa, G. (1986). Akaike information criterion statistics. *Dordrecht, The Netherlands: D.Reidel*, 81.

Schwarz, G. (1978). Estimating the dimension of a model. *The annals of statistics*, *6*(2), 461-464.

Silverwood, R. J. (2008).

Issues in modelling growth data within a life course framework.

Simondon, K. B., Simondon, F., Delpeuch, F., & Cornu, A. (1992). Comparative study of five growth models applied to weight data from congolese infants between birth and 13 months of age. *American Journal of Human Biology*, *4*(3), 327-335.

Stang, J., & Story, M. (2005). Adolescent growth and development. *Guidelines for adolescent nutrition services*, *1*(6).

Stützle, W., Gasser, T., Molinari, L., Largo, R., Prader, A., & Huber, P. (1980). Shape-invariant modelling of human growth. *Annals of Human Biology*, *7*(6), 507-528.

Tanner, J. M. (1962). Growth at adolescence.

Tanner, J. M. (1981). Growth and maturation during adolescence. *Nutrition reviews*, *39*(2), 43-55.

Tanner, J. M. (1990). *Foetus into man: Physical growth from conception to maturity.* Harvard University Press.

Team, R. C. (2013). R: A language and environment for statistical computing.

Tzoulaki, I., Sovio, U., Pillas, D., Hartikainen, A.-L., Pouta, A., Laitinen, J., ... Elliott, P. (2010). Relation of immediate postnatal growth with obesity and related metabolic risk factors in adulthood: the northern finland birth cohort 1966 study. *American Journal of Epidemiology*, *171*(9), 989-998.

van Dommelen, P., van Buuren, S., Zandwijken, G. R., & Verkerk, P. H. (2005). Individual growth curve models for assessing evidence-based referral criteria in growth monitoring. *Statistics in medicine*, *24*(23), 3663-3674.

Viner, R. M., Ross, D., Hardy, R., Kuh, D., Power, C., Johnson, A., ... Batty, G. D. (2015, Aug). Life course epidemiology: recognising the importance of adolescence. *Journal of epidemiology and community health*, *69*(8), 719-720. doi: 10.1136/jech-2014-205300[doi]

WHO. (2004). Global strategy on diet, physical activity and health.

WHO. (2018). *Obesity and overweight.* (`http://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight`)

Wingerd, J. (1970). The relation of growth from birth to 2 years to sex, parental size and other factors, using rao's method of the transformed time scale. *Human biology*, 105-131.

Wong, D. L., & Wilson, D. (1995). *Whaley and wong's nursing care of infants and children.* Mosby.

Appendices

R-Codes

```
# Required libraries

library(nlme)

library(sitar)

library(splines2)

library(MASS)

######### Final models used for fitting the females' data (Table 3.10) ############


# Jenss-Bayley model

WghtJB.females.nls <-nls(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5)),
                          data=females_centered_5,
                          start=c(a0=1,b0=1,c0=1,d0=1), na.action=na.exclude)


WghtJB.females.nlme1 <-nlme(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5)),
                             data=females_centered_5,
                             fixed=a0+b0+c0+d0~1,
                             random=a0~1|IDME,
                             start=c(a0=14.659,b0=4.540,c0=-12.728,d0=1.374),
                             na.action=na.exclude)


WghtJB.females.nlme2 <-nlme(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5)),
                             data=females_centered_5,
```

```
                              fixed=a0+b0+c0+d0~1,
                              random=a0+b0~1|IDME,
                              start=c(a0=14.4,b0=4.5,c0=-12,d0=1.3),
                              na.action=na.exclude)

anova(WghtJB.females.nlme1,WghtJB.females.nlme2)

# Reed 1st order model
WghtReed1.females.nls <-nls(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                              (d0*Centered_5_Inverse),
                              data=reed_females_centered_5,
                              start=c(a0=1,b0=1,c0=1,d0=1), na.action=na.exclude)

WghtReed1.females.nlme1 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                                (d0*Centered_5_Inverse),
                                 data=reed_females_centered_5,
                                 fixed=a0+b0+c0+d0~1,
                                 random=a0~1|IDME,
                                 start=c(a0=-.7,b0=2.8,c0=12.3,d0=19.1),
                                 na.action=na.exclude)

WghtReed1.females.nlme2 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                                 (d0*Centered_5_Inverse),
                                 data=reed_females_centered_5,
                                 fixed=a0+b0+c0+d0~1,
                                 random=a0+b0~1|IDME,
                                 start=c(a0=.08,b0=2.8,c0=11.8,d0=17.8),
                                 na.action=na.exclude)

anova(WghtReed2.females.nlme1,WghtReed2.females.nlme2)
```

```
# Reed 2nd order model
WghtReed2.females.nls <-nls(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                            (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                            data=reed_females_centered_5_exclude,
                            start=c(a0=1,b0=1,c0=1,d0=1,e0=1), na.action=na.exclude)

WghtReed2.females.nlme1 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                               (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                               data=reed_females_centered_5_exclude,
                               fixed=a0+b0+c0+d0+e0~1,
                               random=a0~1|IDME,
                               start=c(a0=-68.5,b0=-0.77,c0=52.4,d0= 134.9,e0=-43.1),
                               na.action=na.exclude)

WghtReed2.females.nlme2 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                               (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                               data=reed_females_centered_5_exclude,
                               fixed=a0+b0+c0+d0+e0~1,
                               random=a0+b0~1|IDME,
                               start=c(a0=-72.9,b0=-0.9,c0=54.9,d0=143.02,e0=-46.8),
                               na.action=na.exclude)

anova(WghtReed2.females.nlme1,WghtReed2.females.nlme2)

WghtReed2.females.nlme3 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                               (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                               data=reed_females_centered_5_exclude,
                               fixed=a0+b0+c0+d0+e0~1,
                               random=a0+b0+e0~1|IDME,
```

```
                            start=c(a0=-72.04,b0=-0.84,c0=54.09,d0=141.6,e0=-46.27),
                            na.action=na.exclude)

anova(WghtReed2.females.nlme2,WghtReed2.females.nlme3)

# Adapted Jenss-Bayley model
WghtAdptdJB.females.nls <-nls(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5))+
                            (e0*(Centered_5_Square)),
                            data=adptd_females_centered_5,
                            start=c(a0=1,b0=1,c0=1,d0=1,e0=1),
                            na.action=na.exclude)

WghtAdptdJB.females.nlme1_centered <-nlme(Weight~a0+(b0*Centered_5)-
                                         exp(c0+(d0*Centered_5)
                                         +(e0*(Centered_5_Square)),
                                         data=adptd_females_centered_5,
                                         fixed=a0+b0+c0+d0+e0~1,
                                         random=a0~1|IDME,
                                         start=c(a0=27.1,b0=1.4,c0=1.8,d0=.2,e0=.9),
                                         na.action=na.exclude)

WghtAdptdJB.females.nlme2_centered  <-nlme(Weight~a0+(b0*Centered_5)-
                                           exp(c0+(d0*Centered_5))
                                          +(e0*(Centered_5_Square)),
                                          data=adptd_females_centered_5,
                                          fixed=a0+b0+c0+d0+e0~1,
                                          random=a0+b0~1|IDME,
                                          start=c(a0=21.4,b0=.9,c0=.16,d0=.3,e0=.6),
                                          na.action=na.exclude)
```

```
anova(WghtAdptdJB.females.nlme1_centered,WghtAdptdJB.females.nlme2_centered)

WghtAdptdJB.females.nlme3_centered  <-nlme(Weight~a0+(b0*Centered_5)-
                                          exp(c0+(d0*Centered_5))
                                          +(e0*(Centered_5_Square)),
                                          data=adptd_females_centered_5,
                                          fixed=a0+b0+c0+d0+e0~1,
                                          random=a0+b0+e0~1|IDME,
                                          start=c(a0=21.4,b0=.6,c0=-.13,d0=.3,e0=.6),
                                          na.action=na.exclude)

anova(WghtAdptdJB.females.nlme2_centered,WghtAdptdJB.females.nlme3_centered)

# SITAR model
strmodel.female9_3<-sitar(x=Age, y=Log_Weight, id=IDME,data=sitar_females_excludeobs,
                         df=3,control=nlmeControl(pnlsTol=.4),
                         fixed='a+b', random='a+c+b')

######### Final models used for fitting the males' data (table 3.11)#######

# Reed 1st order model
WghtReed1.males.nls <-nls(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                         (d0*Centered_5_Inverse),
                         data=reed_males_centered_5_exclude,
                         start=c(a0=1,b0=1,c0=1,d0=1), na.action=na.exclude)

WghtReed1.males.nlme1 <-nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                            (d0*Centered_5_Inverse),
                            data=reed_males_centered_5_exclude,
```

```
                            fixed=a0+b0+c0+d0~1,
                            random=a0~1|IDME,
                            start=c(a0=25,b0=7,c0=-15,d0=-11),
                            na.action=na.exclude)

WghtReed1.males.nlme2 <- nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                            (d0*Centered_5_Inverse),
                             data=reed_males_centered_5_exclude,
                             fixed=a0+b0+c0+d0~1,
                             random=a0+b0~1|IDME,
                             start=c(a0=24.5,b0=7.1,c0=-14,d0=-9),
                             na.action=na.exclude)

anova(WghtReed1.males.nlme1,WghtReed1.males.nlme2)

# Reed 2nd order model
WghtReed2.males.nls <- nls(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                          (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                           data=reed_males_centered_5_exclude,
                           start=c(a0=1,b0=1,c0=1,d0=1,e0=1), na.action=na.exclude)

WghtReed2.males.nlme1 <- nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                            (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                             data=reed_males_centered_5_exclude,
                             fixed=a0+b0+c0+d0+e0~1,
                             random=a0~1|IDME,
                             start=c(a0=27.9,b0=7.3,c0=-16.2,d0=-14.8,e0=1.2),
                             na.action=na.exclude)

WghtReed2.males.nlme2 <- nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
```

```
                            (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                            data=reed_males_centered_5_exclude,
                            fixed=a0+b0+c0+d0+e0~1,
                            random=a0+b0~1|IDME,
                            start=c(a0=39.8,b0=7.9,c0=-23,d0=-35,e0=9),
                            na.action=na.exclude)

anova(WghtReed2.males.nlme1,WghtReed2.males.nlme2)

WghtReed2.males.nlme3 <- nlme(Weight~a0+(b0*Centered_5)+(c0*Log_Centered_5)+
                            (d0*Centered_5_Inverse)+(e0*Centered_5_Square_Inverse),
                            data=reed_males_centered_5_exclude,
                            fixed=a0+b0+c0+d0+e0~1,
                            random=a0+b0+e0~1|IDME,
                            start=c(a0=33.6,b0=7.7,c0=-20,d0=-24,e0=4.5),
                            na.action=na.exclude)

anova(WghtReed2.males.nlme1,WghtReed2.males.nlme2)

# Adapted Jenss-Bayley model
WghtAdptdJB.males.nls<- nls(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5))+
                          (e0*(Centered_5_Square)),
                          data=adptd_males_centered_5_exclude,
                          start=c(a0=1,b0=1,c0=1 d0=1,e0=1), na.action=na.exclude)

WghtAdptdJB.males.nlme1 <- nlme(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5))+
                              (e0*(Centered_5_Square)),
                              data=adptd_males_centered_5_exclude,
                              fixed=a0+b0+c0+d0+e0~1,
                              random=a0~1|IDME,
```

```
                              start=c(a0=19.6,b0=1.7,c0=-7.3, d0=.8,e0=.2),
                              na.action=na.exclude)

WghtAdptdJB.males.nlme2 <- nlme(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5))+
                              (e0*(Centered_5_Square)),
                              data=adptd_males_centered_5,
                              fixed=a0+b0+c0+d0+e0~1,
                              random=a0+b0~1|IDME,
                              start=c(a0=19.7,b0=1.6,c0=-9.3,d0=1,e0=.2),
                              na.action=na.exclude)

anova(WghtAdptdJB.males.nlme1,WghtAdptdJB.males.nlme2)

WghtAdptdJB.males.nlme3 <- nlme(Weight~a0+(b0*Centered_5)-exp(c0+(d0*Centered_5))+
                              (e0*(Centered_5_Square)),
                              data=adptd_males_centered_5,
                              fixed=a0+b0+c0+d0+e0~1,
                              random=a0+b0+e0~1|IDME,
                              start=c(a0=19.6, b0=1.7,c0=-14.7,d0=1.5,e0=.2),
                              na.action=na.exclude)

# SITAR model
strmodel.male9_3 <- sitar(x=Age,y=Log_Weight,id=IDME,data=sitar_males_excludeobs,
                          df=3, control=nlmeControl(pnlsTol=.4),
                          fixed='a+b', random='a+b+c')

################# Diagnostic Testing for females ################

# Fitted values vs standardized residuals
```

```
par(mfrow=c(3,2))
plot(WghtJB.fem$fitted,WghtJB.fem$StdRes, main = "Jenss-Bayley model",
     xlab = "Fitted values", ylab = "Standardized residuals")
abline(0,0)

plot(WghtAdptdJB.fem$fitted,WghtAdptdJB.fem$StdRes,
     main ="Adapted Jenss-Bayley model",
     xlab = "Fitted values", ylab = "Standardized residuals")
abline(0,0)

plot(WghtReed1.fem$fitted, WghtReed1.fem$StdRes,
      ylab="Standardized residuals",
     xlab="Fitted values", main="Reed 1st order model")
abline(0,0)

plot(WghtReed2.fem$fitted, WghtReed2.fem$StdRes,
     ylab="Standardized residuals",
     xlab="Fitted values", main="Reed 2nd order model")
abline(0,0)

plot(strmodel.fem$fitted, strmodel.fem$StdRes,
     ylab="Standardized residuals",
     xlab="Fitted values", main="SITAR model",ylim=c(-30,30))
abline(0,0)

# Age vs standardized residuals

par(mfrow=c(3,2))
plot(WghtJB.fem$Age,WghtJB.fem$StdRes, main = "Jenss-Bayley model",
     xlab = "Age", ylab = "Standardized residuals")
```

```
abline(0,0)

plot(WghtAdptdJB.fem$Age, WghtAdptdJB.fem$StdRes,
     ylab="Standardized residuals",
     xlab="Age", main="Adapted Jenss-Bayley model")
abline(0,0)

plot(WghtReed1.fem$Age, WghtReed1.fem$StdRes,
    ylab="Standardized residuals",
     xlab="Age", main="Reed 1st order model")
abline(0,0)

plot(WghtReed2.fem$Age, WghtReed2.fem$StdRes,
     ylab="Standardized Residuals",
     xlab="Age", main="Reed 2nd order model")
abline(0,0)

plot(strmodel.fem$Age, strmodel.fem$StdRes,main="SITAR model",
     ylab="Standardized residuals",ylim=c(-30,30),
     xlab="Age") # Standardized residuals vs fitted values
abline(0,0)

# Q-Q plots

par(mfrow=c(3,2))
qqnorm(WghtJB.fem$StdRes, main = "Jenss-Bayley model",
      xlab = "Normal Quantiles", ylab = "Standardized residuals")
qqline(WghtJB.fem$StdRes) #adding a line to the qqplot

qqnorm(WghtAdptdJB.fem$StdRes, main = "Adapted Jenss-Bayley model",
```

```
       xlab = "Normal Quantiles", ylab = "Standardized residuals")
qqline(WghtAdptdJB.fem$StdRes) #adding a line to the qqplot

qqnorm(WghtReed1.fem$StdRes, main = "Reed 1st order model",
       xlab = "Normal Quantiles", ylab = "Standardized residuals")
qqline(WghtReed1.fem$StdRes) #adding a line to the qqplot

qqnorm(WghtReed2.fem$StdRes, main = "Reed 2nd order model",
       xlab = "Normal Quantiles", ylab = "Standardized residuals")
qqline(WghtReed2.fem$StdRes) #adding a line to the qqplot

qqnorm(strmodel.fem$StdRes, main = "SITAR model",
       xlab = "Normal Quantiles", ylab = "Standardized residuals",
       ylim=c(-30,30))
qqline(strmodel.fem$StdRes) #adding a line to the qqplot

################# Diagnostic Testing for males ################

# Fitted values vs standardised residuals

par(mfrow=c(2,2))
plot(WghtAdptdJB.male$fitted, WghtAdptdJB.male$StdRes,
     ylab="Standardized residuals",
     xlab="Fitted values", main="Adapted Jenss-Bayley Model")
abline(0,0) #adding a line to the qqplot

plot(WghtReed1.male$fitted, WghtReed1.male$StdRes,
     ylab="Standardized Residuals",
     xlab="Fitted values", main="Reed 1st order model")
abline(0,0)
```

```
plot(WghtReed2.male$fitted, WghtReed2.male$StdRes,
     ylab="Standardized residuals",
     xlab="Fitted values", main="Reed 2nd order model")
abline(0,0)

plot(strmodel.male$fitted, strmodel.male$StdRes,
    main="SITAR model", ylab="Standardized residuals",
     xlab="Fitted values")
abline(0,0)

# Age vs standardised residuals

par(mfrow=c(2,2))
plot(WghtAdptdJB.male$Age, WghtAdptdJB.male$StdRes,
     ylab="Standardized residuals",
     xlab="Age", main="Adapted Jenss-Bayley model")
abline(0,0)

plot(WghtReed1.male$Age, WghtReed1.male$StdRes,
     ylab="Standardized residuals",
     xlab="Age", main="Reed 1st order model")
abline(0,0)

plot(WghtReed2.male$Age, WghtReed2.male$StdRes,
     ylab="Standardized residuals",
     xlab="Age", main="Reed 2nd order model")
abline(0,0)

plot(strmodel.male$Age, strmodel.male$StdRes,
```

```
    main="SITAR model", ylab="Standardized residuals",
    xlab="Age")
abline(0,0)

# Q-Q plots

par(mfrow=c(2,2))
qqnorm(WghtAdptdJB.male$StdRes, main="Adapted Jenss-Bayley model",
       xlab = "Normal Quantiles", ylab="Standardized residuals")
        residuals
qqline(WghtAdptdJB.male$StdRes)

qqnorm(WghtReed1.male$StdRes, main="Reed 1st order model",
       xlab = "Normal Quantiles", ylab = "Standardized residuals")
qqline(WghtReed1.male$StdRes)

qqnorm(WghtReed2.male$StdRes, main="Reed 2nd order model",
       xlab = "Normal Quantiles", ylab="Standardized residuals")
qqline(WghtReed2.male$StdRes)

qqnorm(strmodel.male$StdRes, main="SITAR model",
       xlab = "Normal Quantiles", ylab="Standardized residuals")
qqline(strmodel.male$StdRes)


######### Population predicted level weight growth curves of females #########
         and males superimposed on the observed average weight trajectory

fem_meanwt <- c(21.68,24.25,27.44,36.46,47.54,52.67,56.85)
male_meanwt <- c(22.01,24.75,27.77,36.23,45.96,52.54,62.86)
```

```r
x <- c(6,7,8,10,12,13,15)
fem_observedwt <- data.frame(x,fem_meanwt)
male_observedwt <- data.frame(x,male_meanwt)

par(mfrow=c(2,2))

# Adapted Jenss-bayley model
plot(fem_observedwt$x,fem_observedwt$fem_meanwt,col="red",xlim=c(5,16),
     ylim=c(10,70),main="Adapted Jenss-Bayley model", xlab="Age (years)",
     ylab ="Weight (kg)",type="p",lwd=2)
points(male_observedwt$x,male_observedwt$male_meanwt,col="blue",lwd=2)
lines(spline(females_centered_5_exclude$Age,
      predict(WghtAdptdJB.females.nlme3_centered,
      level=0)),col="red")
lines(spline(adptd_males_centered_5_exclude$Age,
      predict(WghtAdptdJB.males.nlme3, level=0)),col="blue")
legend("bottomright",legend=c("F","M"), col=c("red","blue"),
      bty="o",lty=c(1,1), cex=0.5,text.col="black")

# Reed 1st order model
plot(fem_observedwt$x,fem_observedwt$fem_meanwt,col="red",
     xlim=c(5,16), ylim=c(10,70),main="Reed 1st order model",
     xlab="Age (years)", ylab ="Weight (kg)", type="p", lwd=2)
points(male_observedwt$x,male_observedwt$male_meanwt,col="blue",lwd=2)
lines(spline(reed_females_centered_5_exclude$Age,
     predict(WghtReed1.females.nlme2, level=0)),col="red")
lines(spline(reed_males_centered_5_exclude$Age,
    predict(WghtReed1.males.nlme2,level=0)),col="blue")
legend("bottomright",legend=c("F","M"),col=c("red","blue"),
      bty="o",lty=c(1,1), cex=0.5,text.col="black")
```

```
# Reed 2nd order model
plot(fem_observedwt$x,fem_observedwt$fem_meanwt,
     col="red",xlim=c(5,16),
     ylim=c(10,70),main="Reed 2nd order model",
     xlab="Age (years)", ylab ="Weight (kg)",type="p",lwd=2)
points(male_observedwt$x,male_observedwt$male_meanwt,
       col="blue",lwd=2)
lines(spline(reed_females_centered_5_exclude$Age,
      predict(WghtReed2.females.nlme3, level=0)),col="red")
lines(spline(reed_males_centered_5_exclude$Age,
     predict(WghtReed2.males.nlme3, level=0)),col="blue")
legend("bottomright",legend=c("F","M"), col=c("red","blue"),
      bty="o", lty=c(1,1), cex=0.5,text.col="black")

# SITAR model
plot(fem_observedwt$x,fem_observedwt$fem_meanwt,
    col="red",xlim=c(5,16), ylim=c(10,70),main="SITAR model",
    xlab="Age (years)", ylab ="Weight (kg)",type="p",lwd=2)
points(male_observedwt$x,male_observedwt$male_meanwt,
      col="blue", lwd=2)
lines(strmodel.female9_3,opt="d",yfun=exp, xlim=c(5,16),
     ylim=c(10,70), col="red",xlab="Age (years)",
     ylab="Weight (kg)",main="SITAR model")
lines(strmodel.male9_3,opt="d",yfun=exp, col="blue",xlim=c(5,16),
     ylim=c(10,70),add=TRUE)
legend("bottomright",legend=c("F","M"), col=c("red","blue"),bty="o",
      lty=c(1,1),cex=0.5,text.col="black")

####### Weight velocity curves from the SITAR model for females and males ######
```

```
plot(strmodel.female9_3,opt="v",yfun=exp, xlim=c(5,16),ylim=c(1,7),
     col="red",apv=TRUE, main="SITAR model", xlab="Age", ylab="")
plot(strmodel.male9_3,  opt="v", yfun=exp, col="blue",xlim=c(5,16),
     ylim=c(1,7), apv=TRUE,add=TRUE)
legend("bottomright",legend=c("F","M"), col=c("red","blue"),bty="o",
      lty=c(1,1), cex=0.5,text.col="black")
```