Factors Influencing Growth and Body Composition through Early Adolescence to Young Adulthood

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Declaration

I Howard Lukhanyo Nyati declare that this dissertation is my own work. It is being submitted for the degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University

Signed:  on this 19 day of November 2021

Dedication

This work is dedicated to my late mother who breastfed me with hope and weaned me with perseverance. Her ceaseless prayers and effort to provide a nurturing environment shall forever be the driving force which propels me to reach for my best. Ndinje nje nje ngumama! To my children, Lifa and Sine, sorry for being a partly present father in pursuit of this dream. I will live the rest of my life try to reward the fruit of your sacrifice. To my partner, who's been my number one motivator, the timing of our reunion couldn't have been better. To my siblings, siblings-in-law, nephews and nieces and very dear friends, I couldn't have hoped for a better fighting corner than all of you. You rooted for me through all the jabs and knockout blows, cheering me back to my feet, when all I wanted to do was continue to lie down and submit to a count out. My Maker and my King, thank you for the blessing of life and health, all that I can do is through the strength you give me.

Publication and Presentations Arising from this thesis

Publications

i. Nyati LH, Pettifor JM, and Norris SA. 2019. The prevalence of malnutrition and growth percentiles for urban South African children. BMC Public Health 2019; 19:492 (Impact factor: 2.837)

JMP and SAN were supervisors and contributed to initial conceptualization with LHN, editing and sign-off. LHN analysed the data and generated the first draft and revisions.

ii. Nyati LH, Pettifor JM, Ong KK, and Norris SA. 2020. Adolescent growth and BMI and their associations with early childhood growth in an urban South African cohort. American Journal of Human Biology 2020; e23469. DOI: 10.1002/ajhb.23469 (Impact factor: 1.558)

JMP and SAN were supervisors and contributed to initial conceptualization with LHN, editing and sign-off. LHN analysed the data and generated the first draft and revisions KKO contributed to editing and sign-off

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Oral - Nyati LH, Pettifor JM, Ong KK, and Norris SA. The effect of early life growth on the size, tempo and velocity of adolescent growth. Department of Paediatrics Research Day, School of Clinical Medicine, University of the Witwatersrand, Johannesburg, South Africa; December 2017

Oral - Nyati LH, Pettifor JM, Ong KK, and Norris SA. The Effect of the Size, Tempo & Velocity of Pubertal Growth on Adult Body Composition & Size. Nutrition & Growth Conference, Paris, France; March 2018.

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Cambridge PhD Exchange Programme (June – September 2016): As part of the PhD, I participated in the UK Royal Society & SA PhD exchange programme which allowed me to spend 3 months at the University of Cambridge, United Kingdom. Through this programme I had the opportunity to work with Profs Ken Ong and Tim Cole, who helped develop my skills in epidemiology and SITAR modelling.

Abstract

Objectives

Obesity is a global pandemic, and its rise is associated with a higher risk of non-communicable diseases (NCD). The prevalence of obesity is rising faster in low- and middle-income countries (LMIC) contributing to an epidemiological transition from communicable to NCD. A life-course approach can give insight into critical periods during which increases in obesity incidence occur and changes in adolescent body composition may be associated with adult obesity. Therefore, the aims of this thesis in a cohort of South African urban children were, to (i) assess age-related changes in the prevalence of overweight and obesity and growth and comparing percentiles between race groups and international reference; (ii) characterise racial differences in height, weight and body mass index (BMI) during adolescence; (iii) assess the association between early childhood growth and the magnitude, timing and intensity of adolescent growth; (iv) assess the association between the magnitude, timing and intensity of adolescent growth and young adult body composition; (v) assess the association between adolescent BMI and adult body composition in relation to biological maturity.

Methods

This thesis analysed data from prospective longitudinal Birth to Twenty Plus (Bt20+) cohort. A total of 5449 children born in the City of Johannesburg municipal region of South Africa from

the 23rd of April to the 8th of June in 1990 were screened for enrolment. A total of 3273 (78% black, 12% coloured, 4% Indian & 6% white) singleton newborns with no congenital defects, born to mothers who had permanent residence or continued residence for 6 months were included in the study.

Anthropometric data were collected from birth to 24 years using standard techniques. Dual x-ray absorptiometry (DXA) was used to measure body composition (whole body and abdominal fat mass and whole-body lean mass) from age 21 to 24 years. Data were converted to age and sex specific z-scores for height (height-for-age, HAZ), weight (weight-for-age, WAZ and weight-for-length, WHZ) and BMI (BMI-for-age, BMIZ) using the World Health Organisation (WHO) 2006 child growth standards to determine the prevalence of stunting, underweight and wasting using the cut-off of -2SDs, from birth to 5 years. Overweight and obesity from 2 to 18 years was determined using the age- and sex-specific cut-offs from the International Obesity Taskforce (IOTF). The lambda, mu and sigma (LMS) method was used to generate age- and sex-specific percentiles for height, weight and BMI from 2 to 19 years. Longitudinal changes in anthropometric characteristics (height, weight and BMI) were modelled using the superimposition by translation and rotation (SITAR) method from age 7 to 23 years. The model summarised growth using three random effects; size (magnitude), tempo (timing) and velocity (intensity). Associations between growth in early childhood and growth in adolescence, as well as between growth in adolescence and body size & composition in adulthood, were assessed using linear regression models.

Results

There were ethnic and sex differences in the prevalence of early childhood undernutrition and overweight and obesity in adolescence. Black males had the highest prevalence of stunting (34.4%) at 2 years of age, compared to 16.7%, 24.9% and 0.0% in white males, black females and white females, respectively. Black females had the highest prevalence of overweight/obesity (46.5%) at 21+ years compared to 26.1%, 14.9%, and 29.4% in white females, and black and white males respectively. The 50th percentile for height for black males was similar to the 10th percentile for South African white males and CDC reference. The 50th percentile for waist circumference for black females approached the 10th percentile of the NHANESIII reference while the 50th percentile for BMI and weight for black females was similar to the 50th centile of CDC reference. Black males also experienced an 8-month delay in the timing of age of peak height velocity (APHV) compared to white males, while black females had a 3-month earlier APHV than white females. Early childhood growth explained a greater variance of the magnitude of the adolescent growth spurts for height, weight, and BMI (range: 19.3 to 52.3%) than it did for timing (range: 5.5 to 15.2%) and intensity (range: 2.1 to 10.8%). In turn, the magnitudes of adolescent weight and BMI gain were the strongest predictors of young adult BMI, fat mass, fat-free soft tissue mass, fat mass index (FMI) and fat-free soft tissue mass index (FFMI), than the timing and intensity of weight and BMI. Adolescent weight was also positively associated with young adult height. Achieving peak weight gain before APHV was associated with greater fat mass and FMI than after APHV in females. Childhood onset overweight/obesity is associated with greater BMI, whole body and trunk fat mass percent than late adolescence onset overweight/obesity

Conclusion

This thesis used a lifecourse approach to address two important global health problems which are plaguing LMIC, the persistently high prevalence of undernutrition and the emerging obesity pandemic. There are additional periods of growth faltering and residual plasticity in black children. Thus, there are several windows of opportunity to influence growth: 1) in foetal/infancy and prepubertal periods to promote optimal linear growth, 2) childhood to early adolescence to prevent unhealthy and persistent body mass gain, and 3) late adolescence to prevent the resurgences of weight and BMI velocities in women. Long-term (childhood onset) obesity could have more adverse effects for cardiometabolic disease risk than late adolescent onset obesity.

Acknowledgements

This research was made possible by the funders of the Birth to Twenty Plus cohort (Bt20+) and the SAMRC/Wits Developmental Pathways Research Unit. I wish to thank my supervisors, Profs John Pettifor and Shane Norris, who gave me the opportunity to take this journey and patiently supported me through the learning process. Their teaching and sound advice have made an invaluable contribution to my development. Thank you also to Dr Simon Schoenbuchner who patiently introduced me to SITAR modelling and R programming and Prof Tim Cole for his availability to answer many questions that helped me understand the modelling better. Thank you also to my dear friends, Drs Rihlat Said-Mohamed and Ansuyah Magan who helped with editing of the thesis. Thank you also to Ms Cynthia Smith who assisted with the Turnitin report even on weekends and odd times. I wish to acknowledge the past and present staff of the Bt20+ cohort for their tireless effort in ensuring the collection and quality of the data. Lastly, I dedicate this work members of the Bt20+ cohort and their parents, the true heroes of this landmark cohort.

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Preface

This doctorate began with a curiosity on learning and applying a new technique to model the growth of children from the Birth to Twenty Plus (Bt20+) cohort. The superimposition by translation and rotation (SITAR) growth curve model had at the time been applied to characterise ethnic (racial) and sex differences in the development of bone age during puberty. Despite an impressive list of publications describing the anthropometry of children from the cohort, the adolescent growth spurt had not been characterised. Having previously analysed data from this cohort from my Master of Science degree, looking at racial differences in the growth of the axial and appendicular skeletons, the idea to work on longitudinal data was a great opportunity to be part of a novel activity in the context of South African and Africa as whole.

There is paucity of cohort studies in Africa and the adolescent growth spurt of African children is not well described. It is not that the growth of African children had not been studied. South Africa has a long history of growth studies dating as far back as the late 1930's (Kark and le Riche, 1944). However, the majority of studies were cross-sectional, and few studies have tracked the growth of children longitudinally (Richardson, 1978; Wagstaff et al., 1987; Charning-Pearce and Solomon, 1988; Cameron et al., 1994); none covered the entire postnatal period from birth to maturity. Longitudinal growth studies "form a large share of the evidence base for much of the knowledge on normal growth of children" (Himes et al., 2006).

This study promised to fill that gap using data from the largest and longest running study of child health in Africa. The biggest attraction for me was the opportunity to learn a new skill and the

challenge of applying it to such a renowned dataset as the Bt20+ cohort. This journey was a challenge for me in many ways. Firstly, longitudinal growth modelling was a new concept, although I had extensive biostatistical knowledge. Secondly, SITAR is only available in the R programming language making the transition from a drop and click statistical package to one based on writing code a huge deal. Never one to run away from a challenge, my journey began with exploring the minefield of code-based data analysis. Learning the methods, tools, application and interpretation has been a long, arduous but fulfilling journey.

One of the important decisions taken at the beginning of this doctorate was not only to look at sex differences but also to disaggregate the analyses by racial classification. Although "race" does not confer biological properties in relation to growth, the history of racial inequality in South Africa warranted the inclusion of race as a factor. There is precedence from this cohort with findings showing a significant difference between black and white boys in the timing of skeletal maturity. The context in which children grow plays a key role in determining growth outcomes. Tanner described child growth a "mirror of the conditions of society". Given the political history of South Africa, racial classification is an important proxy for socio-economic status and residential location. Recent data (2008) show that black South Africans earn only 13% of the annual per capita income of white South Africans. In 1996, 83% of white South Africans were in the top income decile compared to 9% black. Black South Africans have historically been less urbanised than white South Africans.

The impact of this urban environment on changes in body size and body composition during adolescence is not well understood. As previous findings have suggested, adolescence is a

critical period for the development of obesity but the lack of data describing the adolescent growth spurt in children in an urban environment is an important piece of the puzzle to understand the aetiology of obesity which is plaguing all countries in the world, including low- and middle-income countries. The contribution of this thesis is adding this piece of the puzzle from the context of a middle-income country experiencing demographic, nutritional and epidemiological transitions. It is divided into six chapters, with three empirical chapters. Chapter 1 gives an overview of the biological, contextual and developmental determinants of growth and malnutrition. Chapter 2 gives a summary of the methods used in the study, while chapters 3 to 5 give empirical evidence. Chapter 6, which is the last chapter, brings the evidence together, with the aim of providing key take-home messages from this research.

“The success the world has had in protecting children’s rights and realising human potential is captured far more eloquently in flesh and bone than in concrete or steel, far more tellingly in the height of children than in that of skyscrapers”

UNICEF

Chapter 1 Literature Review

1.1 Problem Statement

1.1.1 Obesity Pandemic and the Burden of Disease

Malnutrition is a global health crisis with some declaring obesity a global pandemic (1–3), while the majority of the developing world still grapples with persistently high levels of stunting (4). Globally, the prevalence of obesity is on the rise (***Figure 1-1***) propelled by a positive secular change in body mass index (BMI) in all populations. Data from 200 countries show that age-standardised mean BMI rose by 9.7 and 9.2% between 1985 and 2017 in men and women respectively (5). Consequently, the proportion of adults with a BMI greater than 25 kg/m^2 (overweight & obese) rose from 28.5 to 36.9% for men and 29.8 to 38% for women in a 30-year period (6). Paediatric obesity is also on the rise with 18% (~340 million) of children and adolescents (5 to 19 years) classified as overweight or obese in 2016, globally (7). Among pre-school children, the prevalence of overweight and obesity rose from 4.2% in 1990 to 6.7% in 2010 and was estimated to reach 9.1% in 2020, affecting about 60 million preschool children (8). The latest forecasts suggest that 254 million children (5 to 19 years) will be obese by 2030 (up from 158 million in 2020), with an estimated prevalence of 28 (5 to 9 years) and 27% (10 to 19 years) for children in South Africa, which will be higher than in the United States of America (USA) (9).

Although high-income countries (HIC) such as the USA currently have the highest prevalence of obesity, the epicentre of the pandemic is shifting with low- and middle-income countries (LMIC) increasingly bearing a greater burden of the obesity incidence. The rise in obesity prevalence is faster in LMIC than HIC with the top three countries which had the fastest rise in the last 40 years being in Africa (6,10). It has been estimated of the almost 2 billion overweight and obese individuals worldwide, 62% now reside in developing countries (6). In Africa, sub-Saharan Africa (SSA) is experiencing the highest incidence, with South Africa being among the most affected countries (11). About 35 of the estimated 43 million (81%) overweight and obese pre-school children live in developing countries, with the prevalence higher in Africa than Asia (8).

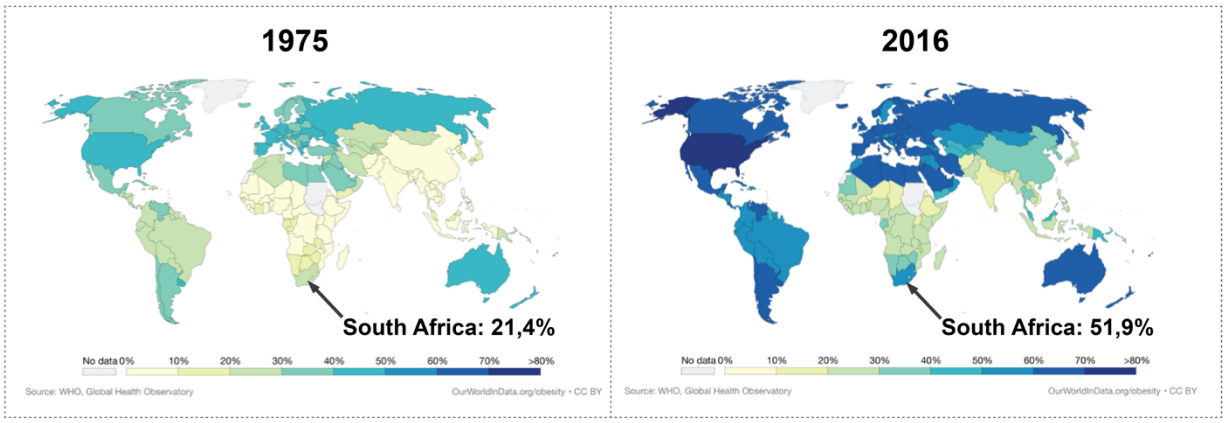


Figure 1-1: Heat map to demonstrate changes in the global prevalence of obesity between 1975 and 2016. Source: Hill et al (12)

Data from the South African National Health and Nutrition Examination Survey (SANHANES) show that males had an average BMI of 23.6 kg/m^2 , which is lower than the global average (5) of 24.4 kg/m^2, while females had an average of 28.9 kg/m^2, which is higher than the global average of 24.7 kg/m^2 (13). Consequently, females had higher a prevalence of combined overweight and obesity than males (63.9% vs 30.7%) (13). Cois and Day found that women had

almost double the change in BMI (+1.82 kg/m^2 per decade vs. +1.03 kg/m^2 per decade) compared to men in a follow-up study between 2008 and 2012 (14). Being a white female from a higher socio-economic stratum was associated with greatest rate of change (14).

As obesity rises, the World Health Organisation (WHO) estimates that the majority of the world population now lives in countries where mortality due to overnutrition surpasses the mortality due to undernutrition (7). The prevalence of obesity is associated the rising burden of noncommunicable diseases (NCD) (15), with overweight and obesity contributing to high mortality (3.4 million) and higher disability (3.8% of disability-adjusted life years) globally (16). A large (over one million) prospective study showed that a BMI over 35 kg/m^2 was associated with two to three times higher risk of mortality related to coronary heart disease (CHD) compared to individuals with a BMI between 18.5 and 24.9 kg/m^2. Data have also shown that the relative risk of developing type 2 diabetes was 42 times (17) and 90 times (18) higher among men and women with a BMI greater than 35 kg/m^2 compared to those with a BMI <22 and < 23 kg/m^2 respectively. LMIC are experiencing an epidemiological transition, where the mortality due to NCD now equals or surpasses that of communicable diseases. However, undernutrition still makes a significant contribution to the mortality burden, with 45% of mortality in children under 5 years being attributed to undernutrition in LMIC (19).

1.1.2 Double Burden of Malnutrition in LMIC

Despite the faster rise in obesity, LMIC are also experiencing a persistent epidemic of undernutrition with 167 of the 171 million children who are stunted living in developing countries (4). Globally, the prevalence of stunting, which is the most common form of undernutrition, decreased by 10% from 39.7 to 26.7% between 1990 and 2010 (4). However, it remains a major problem in developing countries with LMIC in different parts of the world showing different experiences in addressing the prevalence of stunting. While regions like Asia have achieved significant reductions (49 to 28%) over the past 30 years, the prevalence of stunting has remained stagnant in Africa at around 40%, with little prospect of improvement (4). The co-existence of under- and over-nutrition in Africa contributes to a double burden of malnutrition which has significant implications for human capital and population health. The inability to address malnutrition and related NCD will exacerbate the burden on the fiscus in these resource constrained settings. The impact of not acting on malnutrition is estimated to cost between 2.5 and 11.1% of the gross domestic product (GDP), compared to a current expenditure on health as a proportion of GDP of between 2.8 and 9.8% (20).

1.1.3 Double Burden of Malnutrition in South Africa

In keeping with global trends and other SSA countries, the prevalence of overweight and obesity has doubled in South Africa since 1975 (***Figure 1-1***) while the prevalence of stunting has remained stagnant. Although an upper-middle income country according to the World Bank (21), the prevalence of stunting has barely shifted in 20 years between 1994 and 2016 (***Figure 1-2***),

compared to a 5-fold decrease in other upper-middle income countries (22). Similarly, the prevalence of underweight has remained stagnant such that it was higher in South Africa than other upper-middle income countries in 2017, which experienced a significant decline from a higher prevalence in the early 90s (22). South Africa is unique among LMIC and SSA countries due its demographically, economically and socially diverse society.

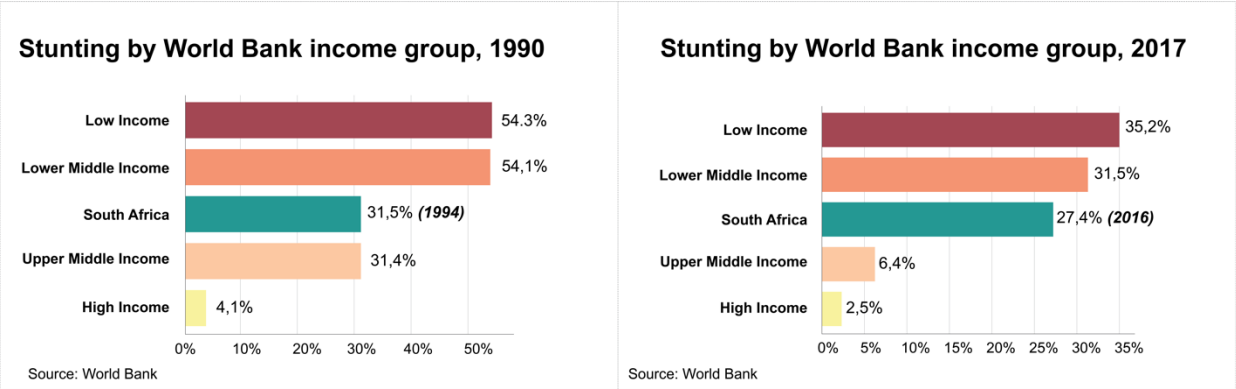


Figure 1-2: Changes in the prevalence of stunting between 1990 and 2016. Source: Roser et al (22)

1.2 Background

1.2.1 Human Growth as a Mirror of the Conditions in Society

Reducing malnutrition requires an understanding of both the biology of normal growth and factors associated with growth failure and excessive weight gain. Child growth is the longest and most energy demanding biological process in the first 18 years of postnatal life (23). Notwithstanding, human growth begins around the ninth week of gestation (24), a period which marks the beginning of the foetal period, when the foetus has attained human features and the foundation for development of human organs and systems has been established (25). The intrauterine growth rate is the fastest in the lifecourse of human development with an average velocity of 82 cm/year. Close to a quarter of adult height is achieved during foetal development under optimal conditions (26,27). Starting off at about 30mm at the beginning of this stage, the foetus continues to grow in size, experiencing rapid growth in length from the third to the fifth month of gestation, while the last two months of gestation are important for changes in weight (24). Approximately 50% of birth weight (~3200 g) is added to the growing foetus in these last two months of gestation (24). The sharp decline in the infant growth velocity for length observed between birth and 1 year follows a peak around the beginning of the second half of pregnancy (***Figure 1-3***).

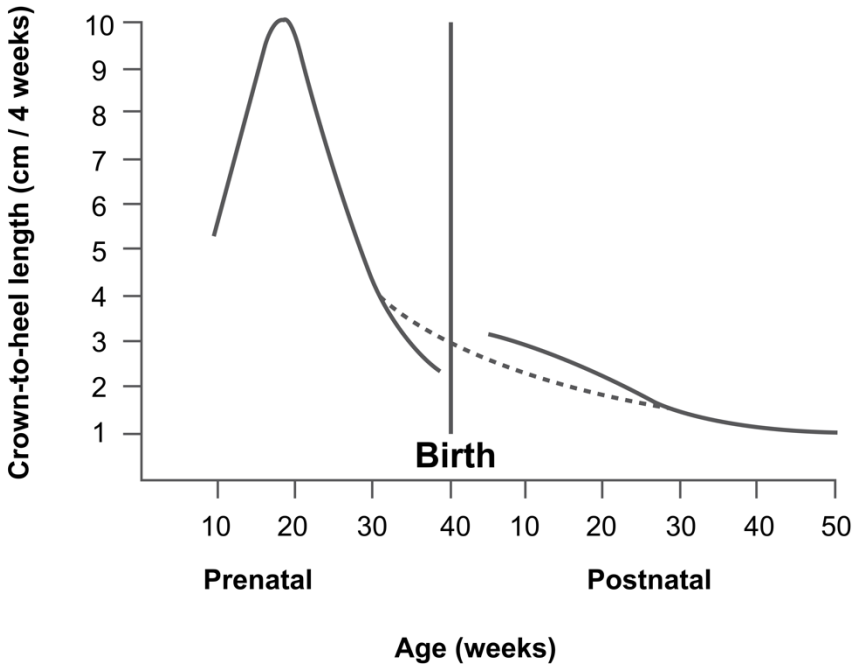


***Figure* 1-3: Velocity for crown to heel length expressed as growth in cm per 4 weeks of gestation. Source: Tanner** (28)

Generally, the postnatal growth rate is on a net decline, being interrupted by an increase during the adolescent growth spurt before another sharp decline towards growth cessation (***Figure 1-4***). Although a continuous process, postnatal growth is stratified into four distinct phases, infancy, childhood, juvenile and adolescence (29). These stages are biologically and mathematically distinguishable by marked differences in the growth velocity. The most rapid postnatal growth velocity is observed in infancy, followed by a long period of slow, constant velocity between childhood and the juvenile period, which extends the human growth period longer than expected for a primate of its size (29). Childhood is followed by adolescence, which is another period of rapid growth, with dynamic increases in height and weight and development of secondary sexual

characteristics during puberty. Adolescence is the only postnatal period during which the growth velocity for height rises.

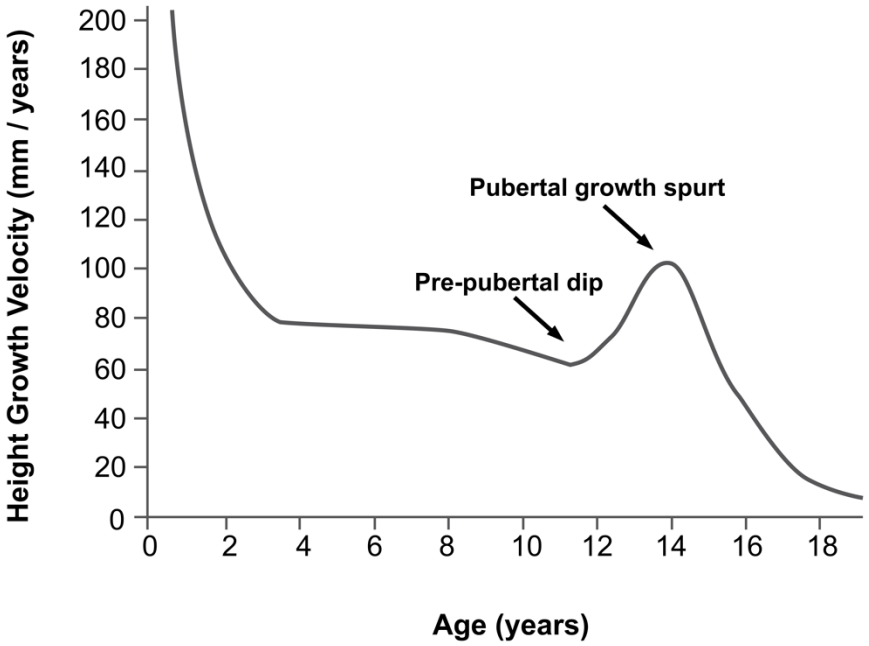


Figure 1-4: Human growth velocity growth curve to demonstrate the phases of the human growth lifecycle. Source: Haymond et al (30)

1.2.1.1 Critical Periods of Growth – Pregnancy & Infancy

There are population differences in the timing of the phases, the velocity of growth and the size attained during the phases, influenced by environmental factors. Child growth is the most sensitive indicator of health and the social environment, with economic and societal conditions being acutely reflected in the heights of children and adults. The sensitivity of child growth to environmental cues may be influenced by the growth velocity, with increased vulnerability to

adverse environmental effects during periods of fast growth and development, such as pregnancy, the infancy period and potentially adolescence. Data assessing the impact of the Dutch famine on birth outcomes show that acute maternal nutritional deprivation during the first and second trimester was more strongly associated with poor birth outcomes than deprivation during the third trimester (31), when the growth velocity is on a decline. Epidemiological evidence which shows a negative association between birth weight and the risk of cardiometabolic disease demonstrate the long-term effects of growth failure during pregnancy (32,33).

These data formed the basis for the formulation of the foetal programming theory by David Barker, which purports that adverse environmental changes during critical periods of pregnancy may permanently alter the physiology and morphology of the growing foetus, with long term consequences for growth and health (32,33). However, the vulnerability of growth beyond the pregnancy period has been demonstrated. Data show that children from LMIC experience growth faltering in infancy which reaches a trough at the age of 2 years, when the prevalence of undernutrition is the highest (34). Although infants from LMIC display average birth lengths which are close to those of infants from HIC (35,36), they experience growth faltering in infancy. The pattern of growth faltering is greater in Africa and South East Asia (***Figure 1-5***) (37), which have been most affected by food insecurity (38) and poor WASH conditions (39).

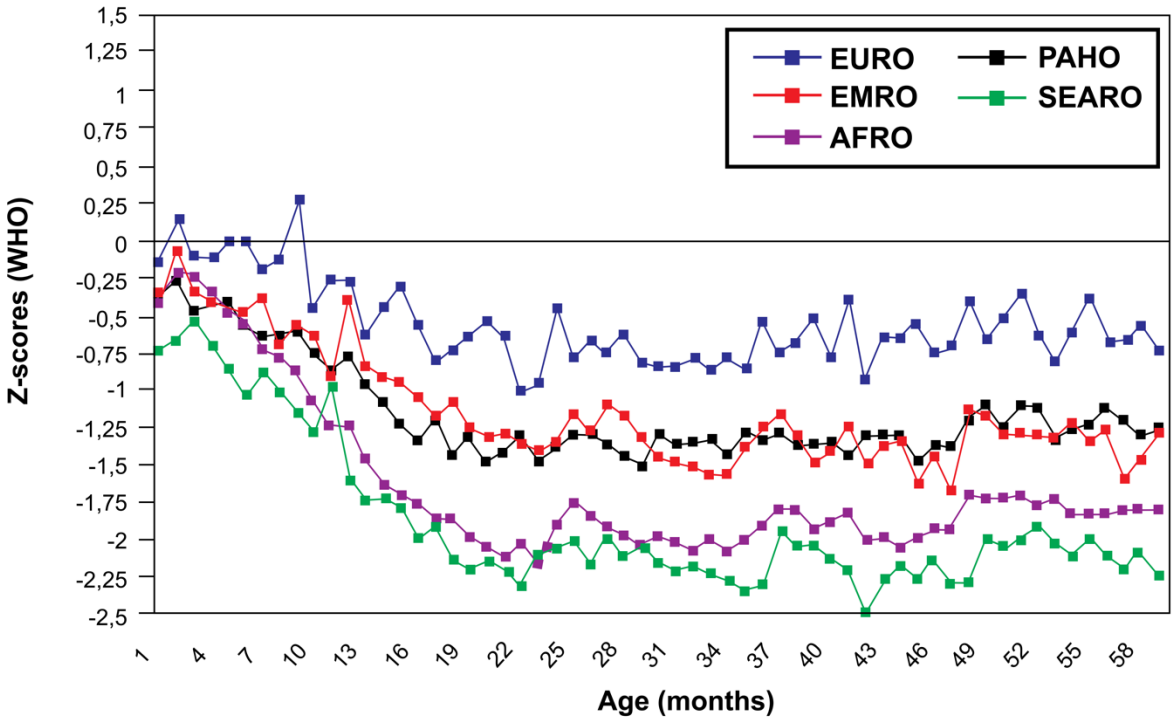


Figure 1-5: Change in height for age z-scores from LMIC in five global regions: Europe and Central Asia (EURO); North Africa and the Middle East (EMRO); sub-Saharan Africa (AFRO); Latin America and the Caribbean (PAHO/AMRO) and South Asia (SEARO). Source Victora et al (37)

Data from five LMIC cohorts (***Figure 1-6***), including the Birth to Twenty Plus (Bt20+) cohort from South Africa, as well as cohorts from Brazil, Guatemala, India and Philippines show that this decline occurs regardless of family socio-economic status (SES) (34). Dagan et al also indicated that this pattern is present among infants of "normal or close to normal nutritional status" (40). This pattern of growth has led to the suggestion that the first two years of life represent the period of greatest vulnerability to environmental stresses, postnatally. Consequently, the foetal programming theory has been revised to the more inclusive developmental origins of health and disease (DOHaD) theory, which recognizes periods

preceding and beyond pregnancy as critical periods for the developing offspring, with transgenerational effects dating back to the conception of the mother by the maternal grandmother (41,42). In this theory, the first thousand days of life, which covers the period from conception to the end of the first two years postnatally, is considered a critical period with high developmental plasticity.

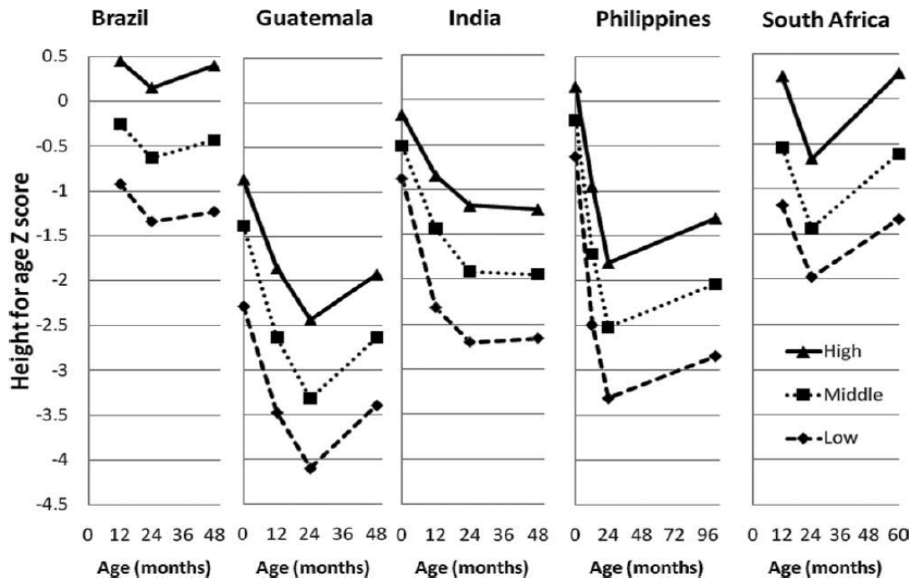


Figure 1-6: Comparison of early childhood growth patterns between five cohorts from LMIC. Source: Stein et al (34)

The sensitivity of height to adverse environmental cues can be explained by the life history theory of a tradeoff, where certain physiological and developmental processes are prioritised over others for the supply of limited energy resources in the body. Thus, during a period of nutritional deprivation there is a tradeoff where brain development is prioritised at the expense of linear growth, in order to improve the chance of reproductive success (43). A cephalocaudal

gradient in growth in which the development of the head (brain) and trunk (vital organs) is prioritized over the legs has been proposed. In 1951, Leitch noted that "...it would be expected on general principles that children continuously underfed would develop into underdeveloped adults...with normal or near normal size head, moderately retarded trunk and relatively short legs" (44). Epidemiological data have shown that leg length is most sensitive to environmental influences (45). Stunting has a multifactorial aetiology but fundamentally, inadequate nutrition, chronic diseases and recurrent infections are the principal factors (46,47). The consequence of this tradeoff is the thrifty phenotype, which offers the best chance of survival in the short term by altering physiology to preserve energy, but is associated with increased risk of disease in later life (48).

1.2.1.2 Critical Periods of Growth – Adolescence

Second to infancy, adolescence is a period with the fastest postnatal growth velocity, and it is the only postnatal period when the growth rate rises. Generally, the term adolescence is used to describe the period between the juvenile period and maturity while puberty refers to the biological processes leading to development of secondary sexual characteristics and rapid growth (49). Puberty is a period of dramatic changes in size, body composition, brain plasticity and the development of the sexual reproductive system, making it a potential critical period for malnutrition and the risk of NCD. Thus, adverse environmental changes during this period may predispose to increased risk of disease in later life and possibly the development of future offspring. There is evidence which suggests that brain plasticity during this period allows for recalibration of early life stress through alteration of hypothalamic–pituitary–adrenocortical

(HPA) functioning (50), providing a window of opportunity for intervening in the effects of early life. Epidemiological evidence supporting the suggestion of puberty as a critical period is based on the association between the timing of puberty and cardiometabolic disease risk (51–53). Early puberty is associated with the risk of adult obesity (53,54) and the risk of angina, type 2 diabetes and hypertension after adjustment of SES and body composition (51).

There have also been suggestions that adolescence could provide a window of opportunity to influence adult height (55,56). The reasons for the presence of the adolescent growth spurt in humans is unclear, although a number of theories have been put forward (57). One theory is the concept of "compensatory growth", which suggests that adolescence is a period used to accelerate growth after the slow childhood growth velocity (57) or to compensate for adverse pre-adolescent conditions (55). However, achievement of normal adult stature among children who do not undergo an adolescent growth spurt due to the removal of gonads for medical reasons have questioned the contribution of puberty to adult height (57). Longitudinal data which show a rise in the height deficit, despite improvements in HAZ in adolescence have been used to dispute the contribution of adolescence to adult height (58).

Unlike the inconsistency in its relationship with height, the effect of adolescence and puberty on the adiposity is well established. Early age at menarche is associated with a higher risk of obesity (59) and greater accrual of adiposity (60). Sex differences in the accumulation and patterning of body fat also emerge in adolescence, driven by the influence of sex hormones during puberty. Biologically, there is a predisposition towards fat mass gain in females and lean mass gain in males, driven by hormones (61). This is supported by epidemiological data which show that the

incidence of obesity in girls is almost double that in boys in late childhood and adolescence and is highest in between 11 and 18 years of age among South African females (62). Adolescence is also the period most affected by temporal trends for both height and weight, suggesting an interaction between developmental and ecological factors in the drivers of malnutrition. It has been shown that secular trends in height were greater in the adolescent period than in childhood or post-adolescence (63). Data from South Africa also show that the biggest secular change in BMI between 2008 and 2015 was observed in the peripubertal period (8-11 years of age); higher than any other age group (64). It has also been shown that South African adolescents have experienced a doubling of the prevalence of obesity in a 6-year period (2002 and 2008), which took twice the time (13 years) to develop in the USA (65). Thus, there is a need to understand factors that make the period of adolescence vulnerable to the rise in BMI.

1.2.1.3 Upstream Drivers of Growth Faltering and Excess Weight Gain

Given a similar environment, it is expected that children would grow the same to reach similar adult heights. This is the basis for the 2006 WHO child growth standards, where it was suggested that given healthy growth conditions "children born anywhere in the world have the potential to develop to within the same range of height and weight" (66,67). However, there are notable population differences in child growth and adult height, driven by factors at the individual, household, and societal level. Birth outcomes, developmental milestones and adult body size have a shared socio-economic aetiology, manifesting in differences between countries based on income status (***Table 1-1***). Children from HIC experience better birth outcomes and growth patterns leading to taller adult height and historically higher BMI compared to LMIC (68–72).

Table 1-1: Global variations in developmental milestones, body size and growth parameter:

	Africa		LMIC (excluding SSA)		HIC	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
Birth outcomes						
Weight (g) (69)	Africa region: 3149		Asia: 2713 Central America: 2874		EU (72): 3540[†]	
% LBW (68)	SSA region: 14.0		South Asia: 26.4 Southeast Asia and Oceania: 12.2 Latin America and Caribbean: 8.7		North America, EU, Australia, & New Zealand (Developed): 7.0	
% SGA (73)	SSA region: 25.5		South Asia: 41.5 Southeast Asia and Oceania: 21.2 Latin America and Caribbean:12.5			
Pre-term (74)	SSA region: 12.3		South Asia: Southeast Asia: 24.3 Latin America and Caribbean: 12.5		Developed: 8.6	
Early childhood < 5 yrs						
WAZ at 24m (37)	Namibia: -0.74 Zimbabwe: -0.66 Kenya: -0.97 Ethiopia: -1.34 Cameroon: -0.63 Ghana: -1.58		Brazil: -0.09 Peru: -0.42 Morocco: -0.27 Bangladesh: -2.02 India: -1.84		No data given	
Underweight % 0-59m (75)	Eastern Africa: 14.2 Middle Africa: 13.4 Southern Africa: 8.4 Western Africa: 19.2 Northern Africa: 5.5		Southern Asia: 26.1 Southeastern Asia: 27.2 Latin America and Caribbean: 6.42		No data given	
Overweight % 0-59m (71)	SSA: 3.3		East Asia & Pacific: 6.7 South Asia: 3.1 Latin America and Caribbean: 7.5 Middle East and North Africa: 11.2		North America: 8.8	
HAZ at 24m (37)	Namibia: -1.74 Zimbabwe: -1.16 Kenya: -1.80 Ethiopia: -2.15 Cameroon: -1.45 Ghana: -2.10		Brazil: -0.72 Peru: -1.52 Morocco: -1.29 Bangladesh: -2.42 India: -2.07		No data given	

Stunting % 0-59m (71)	SSA: 33.6		East Asia & Pacific: 11.6 South Asia: 34.4 Latin America and Caribbean: 9.0 Middle East and North Africa: 14.7		North America: 2.6	
WFL at 24m (37)	Namibia: 0.15 Zimbabwe: -0.08 Kenya: -0.06 Ethiopia: -0.33 Cameroon: 0.16 Ghana: -0.66		Brazil: 0.34 Peru: 0.49 (0.60) Morocco: 0.51 Bangladesh: -1.04 India: -1.06		No data given	
Wasting % 0-59 (71)	SSA: 2.3		East Asia & Pacific: 1.6 South Asia: 5.0 Latin America and Caribbean: 0.3 Middle East and North Africa: 3.2		North America: 0.0	
Puberty						
Age of menarche (years)	SSA (76): 14.5 North Africa (76): 13.5 SA (urban) (77): 12.5 SA (rural) (77): 14.5		Philippines (78): 13.1 Colombia (78): 12.8 India (78): 13.5 Brazil (urban) (79): 11.7 Brazil (rural) (79): 11.8		Denmark (80) – 13.0 France (81) – 12.6 UK (82) – 12.9 US (83) – 12.5	
Age of peak height velocity	SA (rural) (84): 14.5 Gambia (85): 16.1	11.8 13.1	India (86): 13.5 Brazil (87): 14.2	10.5 12.4	EU & British (88): 13.9 US (88): 13.6	11.9 11.5
Peak height velocity	SA (rural) (84): 6.54	6.52			UK (89): 10.0	7.7
Adult outcomes						
Height (70)	SSA: 167.3	157.5	Middle East & North Africa: 170.5 South Asia: 165.2	153.3	North America: 176.0 Latvia: 181.4	162.7 169.8
BMI (add reference)	SSA: 20.0 North Africa: 28.0		South East Asia: 22.9 Caribbean: 28 Middle East: 28		Australia: 27.6 North America: 28.4	

[†]crude aggregate based on averaging the means for males and females

1.2.1.3.1 Economic Development and Growth Trends

The taller stature of individuals from HIC has resulted from secular changes attributable to social and economic transitions in those settings. Scientific, medical and industrial advances during the industrialisation period of the 18th century resulted in improvements in the height of Europeans (90), continuing through the 20th century (91). Increments between 3 mm in Scandanavian countries and 30 mm in Southern and Eastern Europe have been observed while in Japan increments of 40 mm were observed from 1950 to 1960 (92). Positive changes in growth have also been observed among children of parents from a LMIC, who are born in a HIC. In one generation, children of Mayan immigrants born in the USA were taller and heavier than Mayan children in Guatemala and Mexico although they were still shorter than African- and Mexican-American children (45).

On the contrary, there is little evidence of a positive secular change in height in LMIC. Akachi and Canning assessed secular changes in 24 SSA countries among cohorts born between 1945 and 1985 (93). They found positive secular changes in Kenya and Senegal while they found changes in Chad and Ethiopia and no trend in the rest of the countries (93). Tobias also found absence of secular trend in South African black males living in Johannesburg and miners between 1919 and 1950 (94). Access to clean drinking water, sanitation and hygiene (WASH) is lacking in many LMIC with SSA and South Asian being the most affected (39). The impact of WASH on growth is well documented, supporting the evidence of the importance of pathogen control on growth. According to the life history theory, resource allocation and pathogen control are two of the most important selection forces for growth (91). The strength of these forces has

been demonstrated even in countries that were historically undergoing the industrialization. Notwithstanding and despite increases in per capita wages in places like the Netherlands, the positive secular trend has been interrupted by periods of decline due to famine (95,96) and increased infections influenced by migration patterns (90), highlighting the competing forces which influence growth.

1.2.1.3.2 Urbanisation and Growth Trends

The social and demographic transitions in LMIC also contribute to within country differences in growth and the prevalence of malnutrition. Community infrastructure (presence of paved roads, markets, or hospitals) is inversely associated with the risk of stunting with the least developed communities having a higher risk than developed communities (97). There are also differences in the prevalence according to location, with rural communities having a higher prevalence than urban communities in LMIC (98). However, despite availability of better facilities, the urban environment alone may not be protective against growth failure and poor child health. Cameron et al found that South African urban children from average SES homes were consistently smaller than rural and well-off urban children (99). An increased level of vulnerability among citizens in the poorer SES stratum has been suggested to reinforce patterns of inequality and poverty in urban societies (100). Over-crowding, which is due to inadequate housing and limited resources in urban areas unable to cope with the influx of migrants, may disproportionately predispose to material deprivation and crime among recent migrants to urban areas (101,102).

Urbanisation is also associated with the prevalence of overnutrition. The global rise in BMI appears to parallel the rise in urbanisation leading to the hypothesis that urbanisation may be a key driver (5). Being of the white population, female, of younger age, and having a higher household income per capita were demographic characteristics associated with greatest rate of change in BMI among South Africans between 2008 and 2012 (14). However, more than 55% of the rise in the global prevalence of obesity between 1985 and 2017 was observed in rural communities (5). SSA is unique in this global trend and among LMIC in that while mean BMI rose faster in rural communities in Asia, the Middle East and north Africa, it rose faster in urban communities in SSA (5). The closing urban-rural gap in LMIC other than SSA is attributed to an urbanisation of the rural areas while it is suggested that urbanisation has preceded broader economic development in SSA (103).

The effects of urbanisation on obesity are influenced by local SES. Domestic rather than global factors are the key drivers of the global upward secular trend in BMI (104). The behaviours that contribute to an obesogenic environment are context specific with contrasting trends between HIC and LMIC. The prevalence is higher in men, rural populations and those in the lower SES in HIC, while it is associated with more affluent urban females especially in SSA. With few exceptions on either side, Del Mar Bibiloni showed that the majority of countries where the prevalence of obesity was 10% higher in females than in males were largely among LMIC, while those where the prevalence was 10% higher in males than females males were largely HIC (105). Also, while obesity has previously been considered an urban disease of opulence, the association of its prevalence with geographical location or individual SES is influenced by country income. Globally, Templin et al found that in the lowest-income countries (up to $10K per capita GDP),

those in the high SES had 3 times or double the rate of obesity than those in low SES while in the richest nations (greater than $40K per capita GDP), the gap was smaller in favour of lower SES individuals (106). Despite the BMI secular trend being greater in white females (14), factors in the urban environment have led to the prevalence of overweight and obesity being higher in black women (107).

1.2.1.4 Downstream Drivers of Growth Faltering and Excess Weight Gain

At the level of the individual, there are also notable differences in drivers of growth (***Table 1-2***) between LMIC and HIC. LMIC are beset with factors which have adverse influences on growth, including low levels of exclusive breastfeeding, inadequate complementary feeding, lower maternal age, increased levels of maternal stress and adverse childhood events with dire consequences for maternal and child health. Although there is a global decline in adolescent fertility, of the 11% births attributed to mothers aged 10 to 19 years, 95% occur in LMIC (108). Children born to younger mothers have double the unadjusted risk of stunting than children born to older mothers in Africa (109). A higher risk of preterm birth and small-for-gestational age (SGA) is associated with younger maternal age (110), and SGA contributes about 20% to risk of stunting (111). Feeding patterns also play a key role in the growth of children. Consumption of protein and calcium rich foods contributes to significant improvements in growth outcomes and gut health (112,113). Notwithstanding, calcium supplementation in late childhood resulted in shorter adult stature in Gambian boys who were habitually on very low calcium intakes in early childhood (114).

Table 1-2: Factors associated with growth at different stages of developmental lifecourse. The tilde symbol (~) means "is associated with"

Stage & Characteristics	Outcome
First 1000 days	
Maternal age	Younger age (< 20 years) ~ SGA (115), stunting (109)
Parity	Nulliparous ~ stunting (115)
Parental size	Short maternal stature ~ SGA, lower birth weight & stunting (115–117) Inter-cristal diameter ~ neonatal length (118) High pre-pregnancy BMI ~ large-for-gestational age & higher body fat at birth (119,120) Maternal undernutrition ~ decreased placental weight (121)
Preconception diet	Higher fat, sugar, takeaway consumption ~ shorter birth length (122)
Gestational weight gain	Excessive weight gain ~ higher fat mass, higher %body fat, higher birth weight, rapid weight gain (123,124)
Placenta size	Changes in transport of fatty acids, amino acids, or glucose through the placenta ~ intrauterine growth restriction (110)
Diabetes	Pre-existing ~ macrosomia (125) Gestational ~ LGA (126) Diagnosed & treated gestational diabetes ~ 35% lower risk of LGA than 1 abnormal OGTT (126)
Mental health	Maternal depression & anxiety ~ poor foetal growth (127) Maternal depression & anxiety ~ preterm birth (128)
Smoking & substance use	~ preterm birth, lower birth length, increased neonatal central adiposity, reduced brain size & function (129,130) ~ Increased risk of obesity (131)
SES	Higher SES ~ maximum gain in infant weight and length (132)
Birth size	Lower birth weight ~ cardiovascular disease and type 2 diabetes (32) Lower birth weigh & rapid late childhood growth ~ hypertension risk (133–135)
Feeding patterns	Regular consumption of milk ~ taller stature in poor community in a MIC (113) Regular consumption of legumes ~ less reduction in HAZ in infancy in a LIC (112) Higher infant and young child feeding index (ICFI) ~ higher HAZ, greater length increment (136) Higher dietary diversity index (DDI) ~ higher HAZ (136) Higher food variety index (FVI) ~ higher HAZ (136) Higher meal frequency index (MFI) ~ greater length increment (136)
Infancy weight gain	Rapid weight gain ~ earlier menarche (137) Rapid weight gain ~ earlier skeletal maturity (138) Rapid weight gain ~ obesity (139)
Childhood to adolescence	
Timing of adiposity rebound	Childhood onset overweight ~ highest risk of adult overweight (140)
Timing of puberty	Earlier onset and faster progression ~ higher adult BMI (54) Earlier puberty ~ increase cardiometabolic disease risk (51)
Adiposity	Higher childhood BMI ~ earlier age of menarche (137) Adolescent onset overweight ~ higher risk of adult overweight than never overweight before early adulthood (140)

1.2.1.5 Lessons from the Bt20+ Cohort, South Africa

Data from the Bt20+ cohort, from which data for this thesis are drawn, have demonstrated the role of maternal factors and household SES on growth. Mother's postnatal depression was associated with increased risk of stunting at 2 years of age (141). Pooled data from the Consortium on Health Orientated Research in Transitional Societies (COHORTS), which includes data from 5 LMIC cohorts (Brazil, Guatemala, India, Philippines, South Africa), including the Bt20+ cohort, showed that maternal height was associated with birth weight, height, and conditional height at different ages, with the strongest associations at 2 years of age (142). In addition, there are generational effects with maternal and paternal birth weight and growth from birth to 2 year each being predictors of offspring birth weight (143). Thus, improving maternal health before and during pregnancy could go a long way in reducing levels of undernutrition and associated adverse health outcomes. With regards to household SES, a higher SES based on a sum of assets, maternal employment, father's completion of secondary education, and employment of a domestic worker, were associated with lower levels of stunting in children below 30 months (144) and at 2 years (145). Preterm birth or being small-for-gestational age (SGA), which are important determinants for growth, were associated with lower educational attainment and less economic success (146).

The growth of children from the Bt20+ cohort have been compared to other cohorts to assess urban-rural differences in the context of LMIC. The patterns in the prevalence of overweight and obesity in black children and adolescents in the Bt20+ cohort could be similar to those observed in a rural sample in South Africa, from Agincourt. Waist circumference was similar between

Agincourt and Bt20+ females, despite shorter stature in the Bt20 female adolescents (77). However, when compared to a rural Lungwena cohort in Kenya, Bt20+ children had greater weight and height velocities than rural Kenyan children (147). This indicates that South Africa may be more advanced in the nutritional transition compared to other countries in SSA, while urban and rural South African populations may be similar. Notwithstanding the similarities in body composition, rural Agincourt female adolescents attained age at menarched 2 years later than Bt20+ females (77).

1.2.2 The Biology of Growth Regulation

1.2.2.1 Chondrogenesis and Linear Growth

The phases of growth correlate with significant biological events associated with human growth. The onset of the childhood phase correlates with the effect of growth hormone (148), while the adolescent growth spurt correlates with the release of sex hormones, testosterone and oestrogen (149). Maturity, identified by the plateauing of the growth curve, signifies the end of growth through epiphyseal plate fusion which is the end process of growth plate senescence (150–152). To achieve growth in height, growth occurs largely in the long bones of the legs, which increase in their length as a percentage of stature compared to the trunk postnatally (153). Histologically growth occurs at the epiphyseal cartilage or growth plate of long bones through the processes of chondrogenesis and endochondral ossification, where cartilage is formed and remodelled into bone (154,155). Anatomically, the growth plate (***Figure 1-7***) is a cartilaginous structure positioned between the metaphysis and the epiphysis at the proximal and distal ends of long

bones. It is divided into three structurally and functionally distinct areas; the resting, proliferative and hypertrophic zones where cartilage formation (chondrogenesis) occurs, driven by cellular processes of proliferation, hypertrophy, apoptosis and ossification. Cell replication occurs in the proliferative zone where chondrocytes form parallel columns, under the influence of the resting zone, to control the direction in which bone elongates (156). Apoptosis which occurs in the hypertrophic zone initiates the process of remodelling where the growth plate is invaded by vasculature leading to the formation of osteocytes in the process of endochondral ossification (bone formation). The development of the growth plate plays a key role in regulating growth velocity. The sharp decline in postnatal growth velocity is attributed to growth plate senescence and it is suggested that a delay in this process is the mechanism behind catchup growth (150).

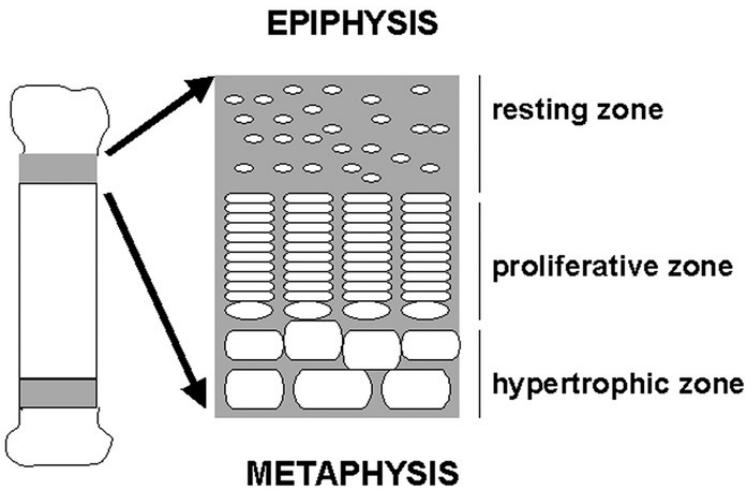


Figure 1-7: Anatomical position and histology of the epiphyseal plate. Source: de Luca (157)

1.2.2.2 Regulation of Chondrogenesis

Generally, postnatal growth is on a net decline from birth to maturity, and this deceleration is attributed to a decline in the proliferation of chondrocytes (151). The mechanisms behind the decline in chondrocyte proliferation, which is the key mechanism for growth plate senescence, is unclear. The decline in the postnatal growth rate is not matched by decreasing concentrations of growth-related hormones. In contrast, the concentration of insulin growth factor-1 (IGF-1) in early childhood, which is a primary effector hormone for postnatal growth, is inversely related to the postanal growth rate (158). The GH/IGF axis, which involves the effector peptide hormones growth hormone (GH), IGF-1, and IGF-2, is the primary signaling pathway for regulating linear growth (157). Both GH and IGF-1 are capable of acting independently in the process of chondrogenesis, with GH stimulating the differentiation of chondrocytes, while IGF-1 stimulates their proliferation (159). GH, which is produced in the anterior pituitary gland and secreted in a pulsatile manner under the influence of the growth hormone release hormone (GHRH) and Ghrelin from the stomach, activates the release of IGF-1 in the liver which also initiates a feedback loop to regulate the release of GH. IGF-1 is also produced in peripheral tissues including the growth plate, suggesting that its regulation of chondrogenesis may involve local or paracrine action (160,161).

However, there is an increase in GH concentrations prenatally, which is not associated with a rise in IGF-1 concentrations. This may be influenced by paucity of GH receptors in fetal tissues during most part of the gestational period (162,163). Prenatally, the actions of IGF-1 and, possibly IGF-2 are influenced by nutritional supplies (161). Resistance to insulin, IGF-I and GH

could be the mechanism by which foetal programming influences the association between foetal growth retardation and postnatal growth failure (164). Postnatally, there is a shift from a paracrine production of IGF to a hepatic production of endocrine IGF-1, stimulated by GH (165,166). A correlation between postnatal GH and IGF-1 concentration signals a shift to GH regulation of IGF-1. The release of GH itself is regulated by other hormones in childhood and adolescence. The mid-childhood growth spurt may be driven by androgens through their interaction with GH. During puberty, the role of GH is complemented by sex steroids, estrogen and testosterone, which contribute 50% to height gained in this period (167). An augmentation to the secretion of GH is also observed in this period. IGF-1 levels also increase during puberty and their concentration is highly correlated with height (167). Thus, sex steroids act by increasing the circulation of GH and IGF-1. Oestrogens act by reducing the IGF-1 mediated feedback of GH, thereby increasing the secretion of GH (167). In males, testosterone mediates the effect of GH on IGF-1 secretion (167). While stimulating growth during puberty in both sexes, oestrogens also contribute to the fusion of the growth plate (161).

1.2.2.3 Adipogenesis and Weight Gain

Unlike height, which slows down as individuals approach the period of growth cessation in late adolescence, weight continues to growth through the lifecourse and critical periods beyond the adolescent period have been suggested (168). Growth in weight exhibits high variability being susceptible to short term changes influenced by behavioral and environment factors. Growth in weight (body mass) is influenced by growth in soft tissue mass (muscle and fat) and bone mass and their growth spurts appear to be synchronized in adolescence (169). A large portion of the

changes in body mass beyond adolescence may be influenced by adipose tissue accrual, which increases the risk of obesity in the older ages. The generation of new adipose tissue cells continues to happen at a substantially high rate even in adulthood (170). Adipose tissue can grow from 2-3% to 60-70% of body mass in response to positive energy balance (171).

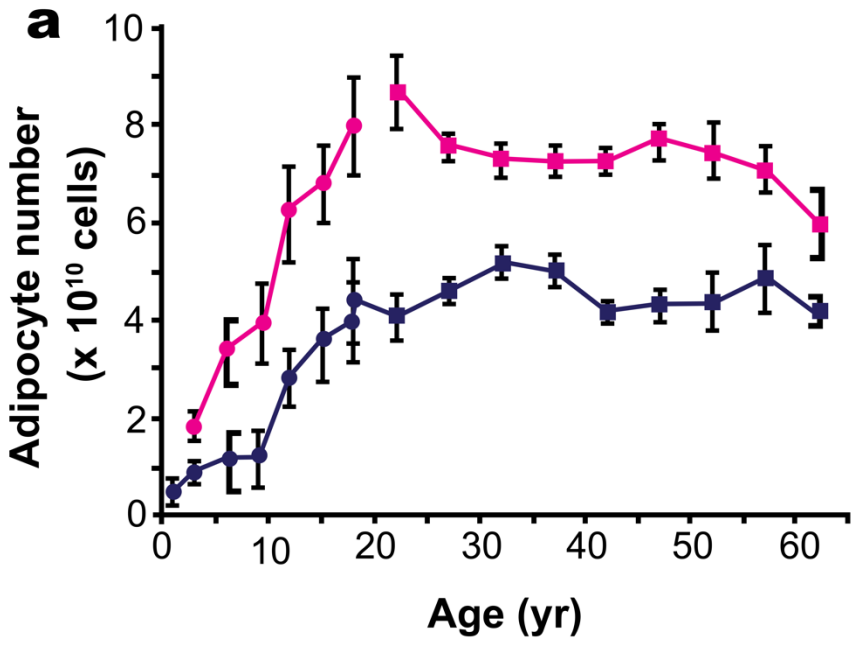


Figure 1-8: Change in number of adipocytes in relation to age in lean (blue) and obese (pink) children (circles) and adults (squares). Source: Spalding (170)

Thus, understanding the drivers of weight gain requires an understanding of the drivers and developmental trajectories of adipose tissue. Obesogenesis is associated with high levels of adipocyte turnover, shortened adipocyte lifespan and an increased rate of apoptosis (172). The growth and expansion of adipose tissue occurs through the processes of hypertrophy and hyperplasia (**Figure *1-8*** & **Figure *1-9***); driven by adipose tissue stem cells, which are present in

various fat depots. Hypertrophy is a process by which an existing adipocyte can increase its volume two to threefold thereby enhancing triglyceride storage. Prolonged hypertrophy is associated with local inflammation and metabolic dysfunction. In contrast hyperplasia, which is the formation of new small adipocytes, is protective against metabolic dysregulation. Experimental studies have shown rapid turnover and replenishment of adipocytes in the early postnatal period while the ability for adipocytes to grow in size is maintained as the organism ages. It is estimated that 8.4% of human adipocyctes are turned over every year (170).

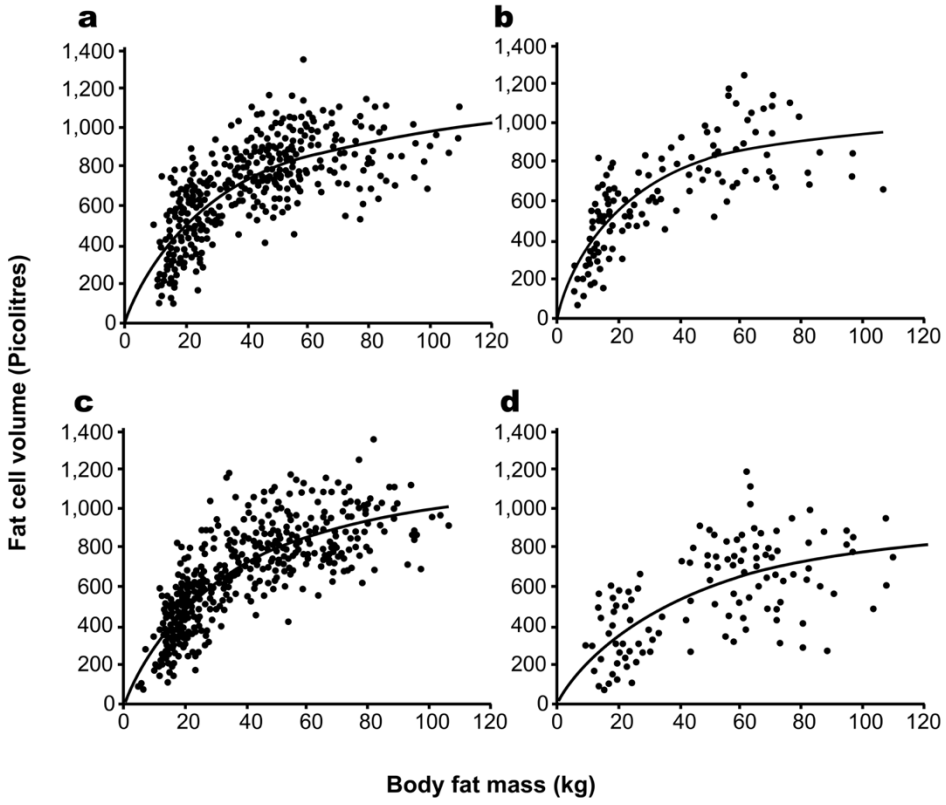


Figure 1-9: Change in the volume of adipocytes in relation to body fat mass in (a) females, (b) males, (c) subcutaneous adipose tissue in both sexes, and (d) visceral fat in males and females. Source: Spalding (170)

Histologically, adipose tissue is divided mainly into white and brown adipose tissue, which have different ontogenic pathways. White adipose tissue (WAT) largely consists of unilocular (one large lipid droplet) cells and is responsible for storing energy. On the contrary, brown adipose tissue (BAT) contains multilocular (multiple lipid droplets) which are responsible for energy expenditure. Activation of BAT may be a potential therapeutic approach in the treatment of obesity. At a gross anatomical level, adipose tissue is subdivided into subcutaneous and visceral depots, distinguishable by anatomical location. The depots also differ histologically, with subcutaneous fat being more heterogeneous, containing both unilocular and small multilocular adipocytes, while visceral fat primarily consists of large unilocular adipocytes.

1.2.2.4 Regulation of Adipogenesis

Fundamentally, nutrition and metabolic balance are the key drivers of weight gain. Adipose tissue is the fastest growing organ in the early postnatal period, possibly due to abundance of lipids in breastmilk in a period of peak milk production in the mother. GH, IGF-1, insulin and leptin along with several others also contribute to the process adipogenesis and fat mass regulation. Adipose tissue is considered the largest endocrine organ and secrete a variety of hormones some of which play a role in appetite regulation. Gonadal hormones play a key role in the initiation of puberty and normal sex dimorphism in the quantity and distribution of adipose tissue in adolescence (173). There is a greater predisposition towards fat mass gain in females and lean mass gain in males (174).

The accrual of fat mass among females in adolescence (and pregnancy) is considered a biological advantage driven to improve fertility and to provide an optimal environment for the development of the foetus and the lactating child (175). It is suggested that efficient fat storage in females is influenced by the action of oestrogen which reduces the postprandial oxidation of fatty acids (176). In addition, energy expenditure (EE) is lower in women than men influenced by height and the quantity of fat-free relative to fat mass. Prepubertal differences in EE may be influenced by the sex chromosomes and the intrauterine organisation of gonadal hormones (175). An increase in both the number and size of adipose cells is observed in adolescence. Adolescent girls undergoing puberty experience a 34% increase in the number of subcutaneous adipose tissue cells in the gluteal region and a 45% increase in adipocyte size compared with similar-aged boys (177–179). Insulin sensitivity also decreases during puberty in both sexes and in obese and non-obese individuals alike. There is a decrease of about 30% in insulin sensitivity during adolescence, attributed to increases in growth hormone (61). Enhanced insulin sensitivity is associated with significant weight reduction (180).

1.2.2.5 Genetic Control of Growth

Genetic and environmental factors play a key role in the control of the biological processes which regulate growth. The hormones and signals which regulate chondrogenesis and adipogenesis are genetically controlled. Evidence for the role of IGF-1 on growth comes from transgenic mice with IGF-1 -/- knockout gene, which exhibit intrauterine growth restriction (161). In humans, intrauterine growth restriction has been observed among patients with IGF-1 and IGF-1 receptor (IGF1R) gene mutations (161). Additionally, genetic epidemiology has

contributed to the evidence of the role of genetics in the regulation of growth. Heritability studies (181) and genome-wide association studies (GWAS) have given insight into the genetic underpinnings of body size and developmental milestones. Phenotypic traits are heritable, and this explains normal morphological variation within a population. GWAS have given insight into the loci involved in the determination of physical characteristics and the variances in the traits associated with those loci (***Table 1-3***). A review of GWAS by Day et al identified several loci involved in the regulation of age at menarche, BMI, height and waist-to-hip ratio with some traits having a shared genetic aetiology (182). However, genetics explain a small portion of the variance in phenotypic traits. A large portion of the variation between populations can be attributed to the environmental factors.

Table 1-3: GWAS studies for the timing of puberty and anthropometric characteristics. Source: Day et al (182)

Reference	Phenotype	Study size	Number of genomic loci (novel loci)	Number of independent signals	Variance explained by top signals
Perry et al (2014)	Age at menarche	182 427	106 (65)	123	2.7
Lock et al (2015)	Adult BMI	339 224	97 (56)	103	2.7
Shungin et al (2015)	Adult waist-to-hip ratio (adjusted for BMI)	224 459	49 (33)	65	2.4% (women) 0.8% (men)
Wood et al (2014)	Adult height	253 288	423 (243)	697	16%

1.2.3 Background on Growth Curve Modelling & Modelling of the Bt20+ Cohort

Growth studies have given insight to the normal variation in body size, growth velocity and the timing of developmental milestones. Thus, growth monitoring is one of the most important tools for public health and has been effectively used to identify children at risk of growth faltering. Characterising the velocity of growth and the timing of developmental milestones is a key element of lifecourse epidemiology. In particular, longitudinal studies of growth and the conditions in which it takes place contribute to our understanding of population trends in malnutrition. Although the growth of South African children has previously been studied, the majority of studies were cross-sectional, and few studies have tracked the growth of children longitudinally (55,183–186). 'A large share of the evidence base for much of the knowledge on normal growth of children' comes from longitudinal growth studies (187).

Considering the growing obesity pandemic, modelling adiposity gain during critical periods of development is essential to our understanding of the biology of adipose tissue gain and whether the timing and velocity of its development is associated with the risk of adult obesity and disease. During adolescence, the timing and velocity of growth is influenced by puberty. The pubertal development of Bt20+ children has been described. The onset of puberty has been estimated to range between 9.8 to 10.5 years of age with over 50% of the cohort reaching Tanner stage 2 of breast, genital and pubic hair development (188). Data have shown racial disparities in the timing of puberty, with black males experiencing 6-month delay in skeletal maturity compared to white males (189). On the contrary, skeletal maturity was similar between black and white females, who also had a similar age of menarche (190). The data show that there was a

secular change towards an earlier age of menarche, from 14.5 in 1956 to 12.4 years of age in the current cohort (190). The age of menarche of Bt20+ females was 2 years earlier than that of a contemporary rural sample from Agincourt (77).

Longitudinal growth modelling has been performed for height and weight in childhood and for pubertal development, skeletal maturity (bone age), metacarpal skeletal growth and BMI in adolescence. Skeletal maturity and skeletal growth were modelled using SITAR (189,191). Chirwa et al examined structural and non-structural models to assess the best fitting model for height and weight between birth and 10 years for age (192). They found that the Berkey-Reed model provided the best fit over the study period. During adolescence, changes in pubertal development for genital, breast and pubic hair development (193), and BMI (194) were modelled using latent class growth analysis (LCGA), which classified children according to the timing and magnitude of development. Lundeen et al found 3 classes for pubic hair development, and 4 classes for breast and genital development in both sexes (193). Munthali et al found 3 classes of BMI for males, and 4 classes for females. Notwithstanding, the adolescent growth spurts for height, weight and BMI have not been described in this cohort.

Describing adolescent growth requires the application of longitudinal growth modelling. Over 200 growth models have been developed (149) with varying degrees of success and limitations (195). Key steps of modelling include firstly, defining parameters which will describe the growth process and secondly, finding a method to assign these parameters to the series of individual measurements (196). Broadly, there are two approaches to human growth modelling, namely the parametric or structural and the nonparametric or non-structural models. In statistical parlance,

the term parametric refers to procedures that make assumptions about the shape of the probability distribution of the population from which the sample is drawn. In modelling, parametric procedures assume an *a priori* model with finite parameters (θ) (197), which capture everything there is to know about the data and assume that the parameters, the predictor (x), and future predictions are independent of the observed values (198). Common nonparametric models are polynomials and splines while parametric models include among others the Berkey-Reed 1st and 2nd order models, Count model, the Infant–Childhood–Puberty (ICP) model, Jenss-Bayley model, and the Preece-Baines model, logistic and the Gompertz (195,199–201).

The various models present with different limitations. Parametric models exhibit model bias, which is a systematic deviation from the underlying biological growth pattern, demonstrated in some cases by the failure to show the mid-growth spurt and enforcing a symmetric adolescent growth spurt (201). They also require the matching of mathematical assumptions with the biological processes being modelled and human growth may not conform to the assumptions in the mathematical models, limiting their ability to describe human growth (202). Gasser et al state that models should have at most five or six parameters and this makes it difficult to find a good model for the growth process from birth to adulthood (201). In addition, choosing an appropriate function to include in the equation for non-linear models may be a challenge (201). Some of the most commonly used parametric models have between 6 and 9 parameters which are largely descriptive with no theoretical justification (201) It is suggested that they are capable of adequately describing a group of children but have may inadequately capture individual variation (201).

Fitting a non-parametric function which allows for more parameters, may circumvent some of the difficulties with parametric models (201). Nonparametric models are useful for curve estimation without an a priori fixed parametric model where the sample parameters are estimated from individual growth curves. Unlike in parametric models where derivates to estimate growth velocity and acceleration are estimated using non-linear least squares (201), using nonparametric smoothing spline functions allows for estimation of age at peak height velocity and peak velocity from the individual curves (196). Additionally, while it may be difficult to estimate derivates from noisy data using parametric models, nonparametric models are designed to reveal the shape of the growth curve hidden in the noisy data and determine the age of occurrence of different features, such as the pubertal spurt (201). Importantly, spline models along with mixed-effects have been found useful in modelling longitudinal data where subjects do not have a consistent number of observations (203,204)

1.3 Conceptual Framework

Longitudinal studies of growth provide an opportunity to assess pathways which may be involved in the risk of obesity and NCD in later life. In the DOHAD framework, several critical periods have been considered for different adult outcomes. Infancy appears to be the most critical period for adult height with little opportunity for positive intervention beyond the first 1000 days of life (58). Using data from the Bt20+ cohort and other LMIC cohorts, Stein et al showed that growth failure in infancy (birth to 12 months) had a stronger association with adult stature and human capital than growth failure in the toddler (12 – 24 months) and late childhood periods (34). Others have also shown that birth weight is independently associated with fat mass

(FM) and fat-free soft tissue mass (FFSTM) in early adulthood, while linear growth between birth and 2 years was strongly associated with visceral adipose tissue (VAT) (205) and FFSTM (206). Notwithstanding, growth between birth and 2 years had a weaker association with fat mass than with FFSTM (206) and no association with glucose intolerance (135). In both studies, it was body size at 4 years which had a stronger association with fat mass (206) and glucose intolerance (135). Others have shown the positive influence of linear growth beyond the first 1000 days, with height at age 7 years being negatively associated with concurrent glucose intolerance (207).

Data have also highlighted the potential role of adolescent growth and puberty to adult outcomes. Data from the Bt20+ cohort have shown that BMI change during adolescence and the timing of puberty are associated with adult body composition and markers of NCD. Being in the early onset obesity & overweight trajectory was associated with a higher risk overweight or obesity in early adulthood (194) as well as higher blood pressure in late adolescent males and females (208). Similarly, the timing of puberty was significantly associated with adult body composition, with being in the early onset puberty trajectory being associated with higher BMI in young adulthood, and this association was independent of prepubertal height and weight (54). Growth is continuous and events in one stage may be influenced by growth in previous stages.

The timing of puberty and adolescent growth are both influenced by childhood growth. Mid-childhood (5 years) height and BMI were associated with earlier onset of pubertal development in the Bt20+ cohort (193). Additionally, rapid weight gain was associated with advanced skeletal maturity (138). Rapid weight gain was also associated greater childhood obesity (139), and having early onset of overweight and obesity and being in the “morbid obese” trajectory (194),

and greater BMI in early adolescence (209). Adolescent growth and pubertal development occur in tandem, and the timing of puberty may influence adolescent growth. It has been suggested that the hypothalamic–pituitary–gonadal axis could be the driver of the adolescent growth spurt. To this end, it has been suggested that comparisons of nutritional status during adolescence should be assessed against age of peak height velocity, which is a marker biological maturity, compared to chronological age which may yield misguided comparisons (210).

The conceptual framework proposed by Bell et al (211) suggests that the timing of puberty is associated with adult cardiovascular and metabolic characteristics through a direct pathway as well as through its effect on adult body composition. The framework also shows a direct link from childhood adiposity to puberty, adult body composition and cardiometabolic traits. This thesis did not measure cardiometabolic traits and childhood growth was measured in early childhood at several time points. Thus, a revised conceptual framework which incorporates prenatal (using birth weight as a proxy) and early postnatal growth is being proposed for this study (**Figure *1-10***).

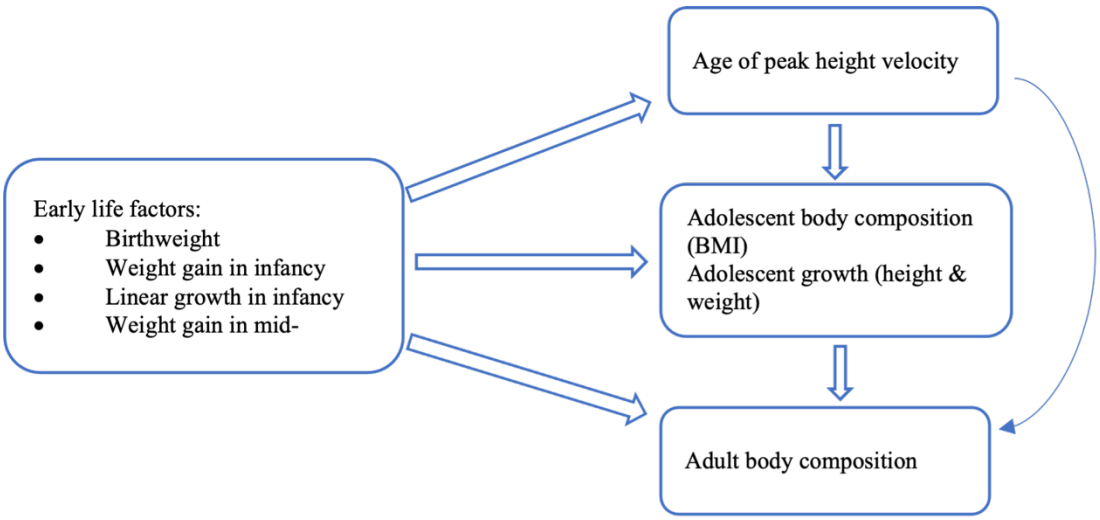


Figure 1-10: A conceptual framework for the association of childhood growth with puberty timing, adolescent growth and adult body composition

1.3.1 Aim:

Therefore, the overall aim of this study was to characterise the growth of black and white South African children and to assess whether adolescent growth patterns may have an independent influence on adult body size and body composition.

1.3.2 Objectives

The objectives of the study were to:

(i) Assess age-related changes in the prevalence of under- and overnutrition and growth patterns and compare percentiles between race groups and international reference.

(ii) Characterise racial differences in height, weight and body mass index (BMI) during adolescence.

(iii) Assess the association between early childhood growth and the magnitude, timing and intensity of adolescent growth.

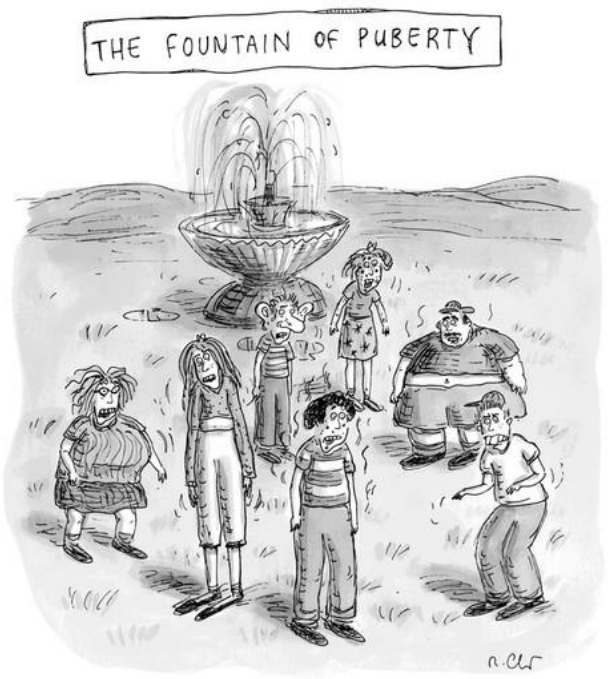
(iv) Assess the association between the magnitude, timing and intensity of adolescent growth and young adult body composition.

(v) Assess the association between adolescent BMI and adult body composition in relation to biological maturity.

1.3.3 Hypothesis

There following hypotheses were tested:

1. White children are taller and heavier than black children.
2. Black males have a delayed timing of the adolescent growth spurt for height and age of peak height velocity
3. A greater magnitude, earlier timing and higher intensity of adolescent weight and BMI are associated with greater adult BMI and whole body and abdominal fat mass
4. A greater magnitude, later timing and higher intensity of adolescent height gain is associated with taller adult height



Source: The New Yorker ©2012

Chapter 2 Study Methods

2.1 Location and Context

This thesis investigated the growth of children enrolled in the Birth to Twenty Plus (Bt20+) birth cohort, which is the largest and the longest running study of child health in Africa. Bt20+ is longitudinal study which followed the growth and development of children in the City of Johannesburg municipal region, South Africa. Johannesburg is the largest city in South Africa and is also the country's economic capital. Although Johannesburg (1645 km^2) covers just 9% of area of the smallest province in South Africa, Gauteng (18000 km^2), the city houses 33% (4 million) of the province's population (12.3 million) (***Figure 2-1***). The demographic breakdown of the city's population is 76 % Black African, 5.6% Coloured, 4.9% Indian/Asian and 12.3% White

Residential location in South Africa under apartheid was determined by racial classification. Apartheid was a system of legislated segregation developed in 1948, which enforced racial separate development (212). Notwithstanding, laws for racial segregation were instituted earlier in 1910, the year South Africa was constituted (213). Spatial planning was designed such that black citizens resided in poor settlements at the periphery of the city, while white citizens resided in opulent suburban areas closer to the city and inner-city residences. Soweto is the largest township (an underdeveloped suburban area) in South Africa with a population of 1.272 million, making up 32% of the population of the CoJ in a 200 km^2 area (214,215).

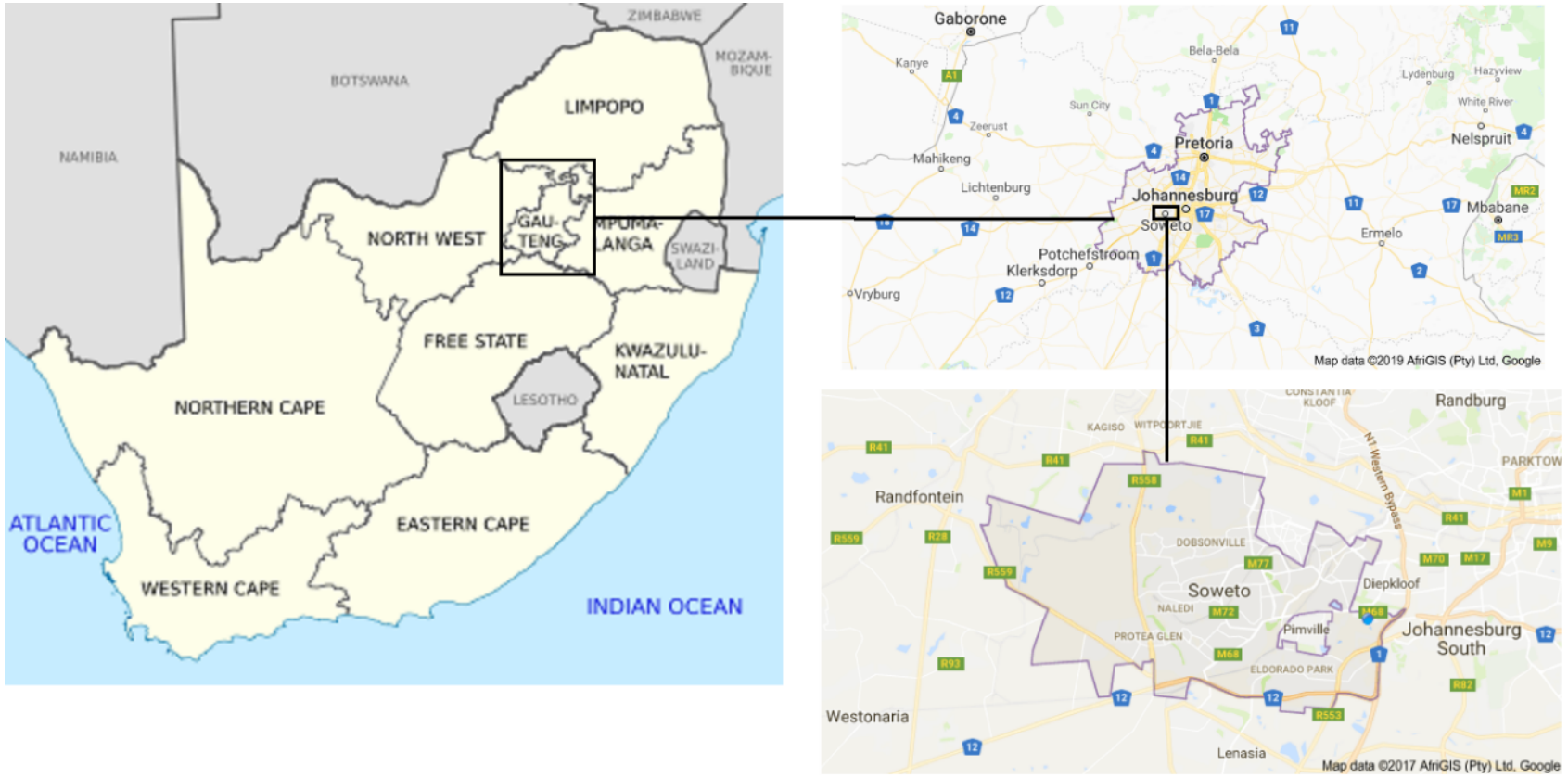


Figure 2-1: Map of South Africa showing the area which the sample was drawn from

Housing comprises of both formal and informal housing with poor or no access to sanitation, electricity, or road infrastructure (

(b)

Figure *2-2*). Soweto was founded in the early 1930s as part of the repressive government's efforts to separate residential areas for black and white under the Urban Areas Act of 1923. Legislated racism was abolished in 1994, after the country's first democratic elections. However, despite the abolishment of the apartheid system, residential location and SES is still largely determined by race, which is a legacy of apartheid.

(a)

(b)

Figure 2-2: Soweto is the largest township in South Africa with both formal but high density (a) and informal (b) housing. Source: https://www.alamy.com/stock-photo/soweto-aerial-view.html (a) & https://stock.adobe.com (b)

2.2 Study Population

The cohort is described fully in references provided (216–218), but a summary is provided here. The children who participated in this cohort were born between the 23rd of April and the 8th of June in 1990, during a period of political transitions in the country. In the same year in February, Nelson Mandela was released from prison after 27 years and later became the first democratic president of South Africa. Of the 5449 children who were born in the Soweto-Johannesburg region (216,219–221), a total of 3273 (black 78%, coloured 12%, Indian 4% & white 6%) mother-child pairs were recruited (217). Inclusion criteria were healthy singleton births and

permanent or continued residence for longer than 6 months in the study area. Initial recruitment took place at antenatal clinics, as well as at delivery, and at 3 months, 6 months, and one year post-delivery (216).

When the children turned 9 years of age, a sub-sample of 429 black and white, boys and girls were recruited from the Bt20+ cohort into a new cohort investigating factors influencing bone mass during late childhood and adolescence, the Bone Health Study. Children diagnosed with asthma, were on medication, as well those who had any condition that may influence bone metabolism were excluded. Because of the small number of white subjects available for inclusion in the Bone Health Study, additional white participants (n= 120) of the same age were recruited from the same schools as the original participants. These participants had similar birth weight, socioeconomic status, maternal age and education to the initial white participants (222)

Self-reported racial classification by the parent was based on government classification which was black (African), coloured (mixed ancestry), Indian (Indian-descent) and white (European-descent). Black South Africans are divided into several tribal groups identified by self-reported home language. Genetically, the tribal groups are largely homogeneous with only a small variation from diverse assortment of ancestral populations (223). There was high attrition among white participants and where possible, analyses were disaggregated by race and sex in this thesis. Ethics approval for the Bt20+ study (M010556) and this thesis (M150108) were provided by the University of the Witwatersrand Committee for Research on Human Subjects. Written informed consent was obtained from parents for all minor children (younger than 18 years), who also gave assent if they were over the age of 11 years of age.

2.3 Physical Examination & Body Composition Assessments

The table below provides a summary of physical characteristics that were used and the format in which they were used. Details for how they were measured are given in each chapter or the reference provided.

2.3.1 Anthropometric Measurements

Measurements were taken during annual visits up to the age of 24 years for weight (from birth), height (from 3 months of age), waist and hip circumferences (from 9 years). In infancy, data were also collected at 3 and 6 months of age. Details for the methods of anthropometric measurements are given in Chapter 3. Data were collected by trained fieldworkers during home visits, between 3 months and 8 years of age, and at the research site from 9 to 24 years. Birth weight was obtained from health records. All measurements were taken in minimal clothing according to standard methods (224,225). Coefficients of variation were used to assess data quality, which were less than 2% for height, 3% for waist and hip circumference.

2.3.2 Body Composition Assessment

Body composition was assessed from age 9 to 24 years by dual x-ray absorptiometry (DXA) on a Hologic QDR 4500A machine. For this thesis, body composition data for ages 21 years and above were used. Details for measurement of body composition are provided in Chapter 5. Bone mineral content (BMC), fat-free mass (FFM), fat mass (FM), abdominal visceral fat (VAT), and

abdominal subcutaneous fat (SAT). Fat-free soft tissue mass (FFSTM) was calculated as the difference between fat free FFM and BMC. A spine phantom was used for daily calibration, and coefficients of variation during the course of the study were less than 1% for total fat mass and fat-free soft tissue mass respectively.

2.4 Growth & Nutritional Classification

2.4.1 Age Group Determination (Chapter 3)

Cross-sectional analyses were performed at each age, which was measured in completed years from 1 to 20 years. Ages 21 to 24 years were included in one age group as 21+. The exact age was used for longitudinal growth models.

2.4.2 Childhood Growth & Nutritional Status

2.4.2.1 Birth and 5 years - Undernutrition

Early childhood nutritional status between birth and 5 years of age was estimated using height-for-age (HAZ), weight-for-age (WAZ), and weight-for-height (WHZ) z-scores, to estimate the prevalence of stunting, underweight and wasting, which are presented in chapter 3. Z-scores were generated using the 2006 World Health Organization (WHO) child growth standards for children between birth and 5 years (67). Participants with HAZ, WAZ and WHZ less than -2

were classified as stunted, underweight and wasted respectively. Biologically implausible values (WAZ < -6 or > 5; HAZ < -6 or > 6; WHZ < -5 or > 5) were excluded from the analyses.

2.4.2.2 Birth and 5 years - Overnutrition

BMIZ were used to assess nutritional status between birth and years. Participants with a BMIZ greater or equal to +1.04, which corresponds to the 85th centile (226), were classified as having overweight and obesity.

2.4.2.3 2 to 21+ years – Thinness and Overweight

The International Obesity Task Force (IOTF) age- and sex-specific cut-offs for children aged 2 to 216 months were used to determine overweight and obesity (227). Adult cut-offs were used for participants older than 216 months. Overweight was defined as BMI >= 25 & < 30 kg/m^2 and obesity as BMI >= 30 kg/m^2.

The International Obesity Task Force (IOTF) age- and sex-specific cut-offs for children aged 2 to 216 months which correspond to the adult cut-offs of < 18.5 kg/m^2 were used to determine thinness. Adult cut-offs were used for participants older than 216 months.

2.5 Statistical Analyses

2.5.1 Data Cleaning

All data handling was performed in latest R software language and environment for statistical computing and graphics (228) and RStudio (229). Data were cleaned by assessing outliers and removing incorrectly captured values. Outliers were assessed using different methods such as box-plot (***Figure 2-3***), flagged z-scores, and the plotclean function in the SITAR version 1.10.11, in R version 3.4.2 (230). During the generation of z-scores, values which were flagged as biologically implausible were excluded from the analyses. Plotclean identifies visible outliers which can be highlighted and removed from the analyses (***Figure 2-4***). Lastly, outliers were identified by modelling data in SITAR and generating standardised residuals. Participants with residual values greater the absolute value of 2 were identified and checked for capturing error.

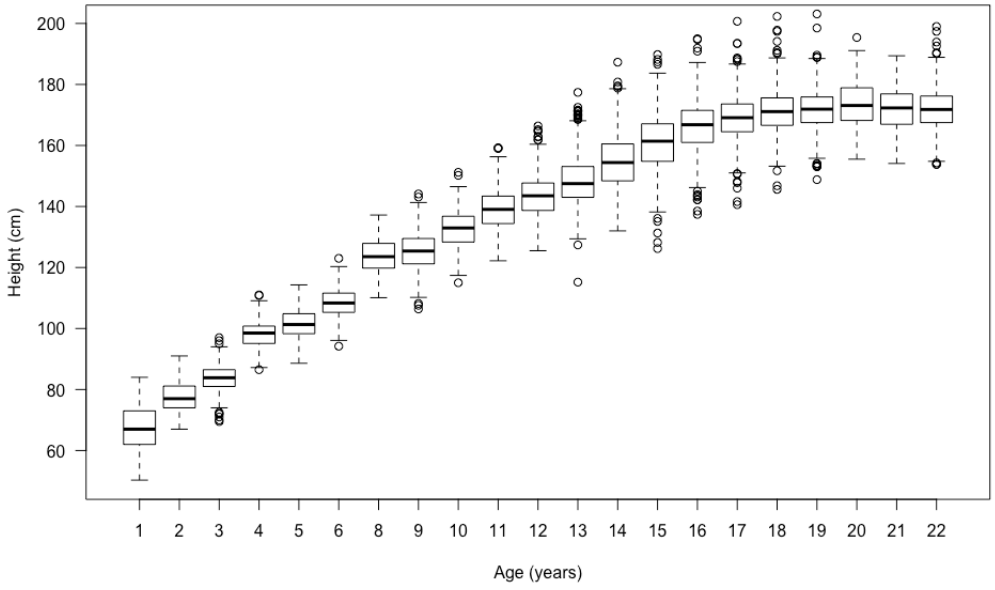
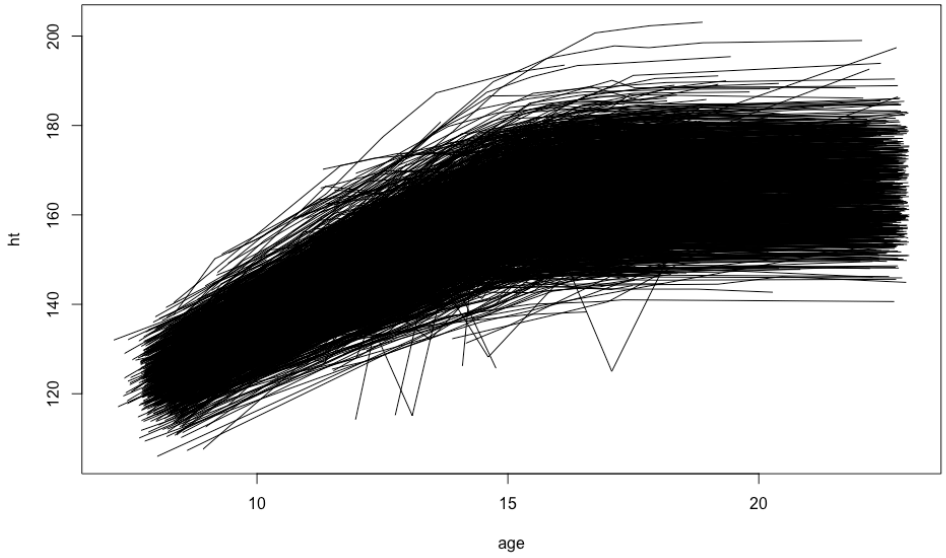


Figure 2-3: Box-plots to demonstrate outliers within each age-group

(a)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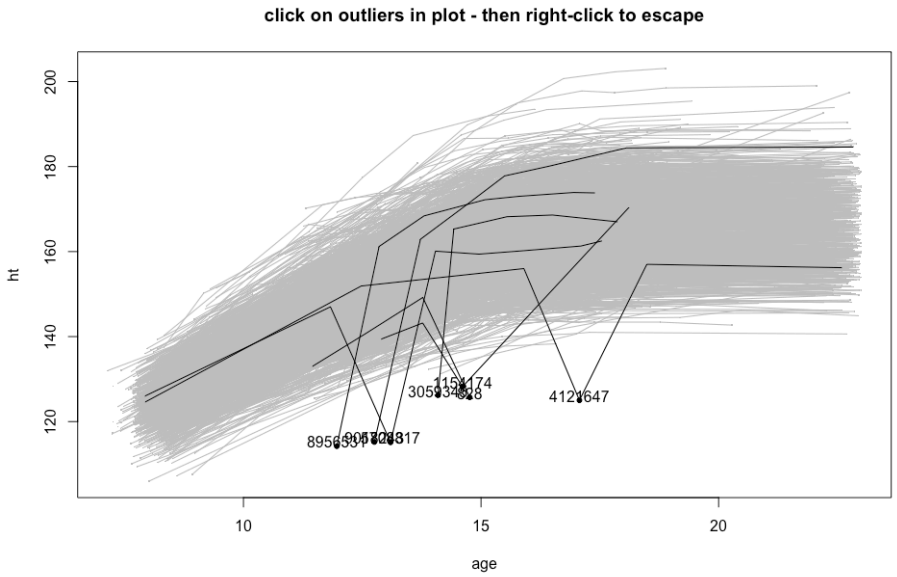
(b)


click on outliers in plot - then right-click to escape
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(c)

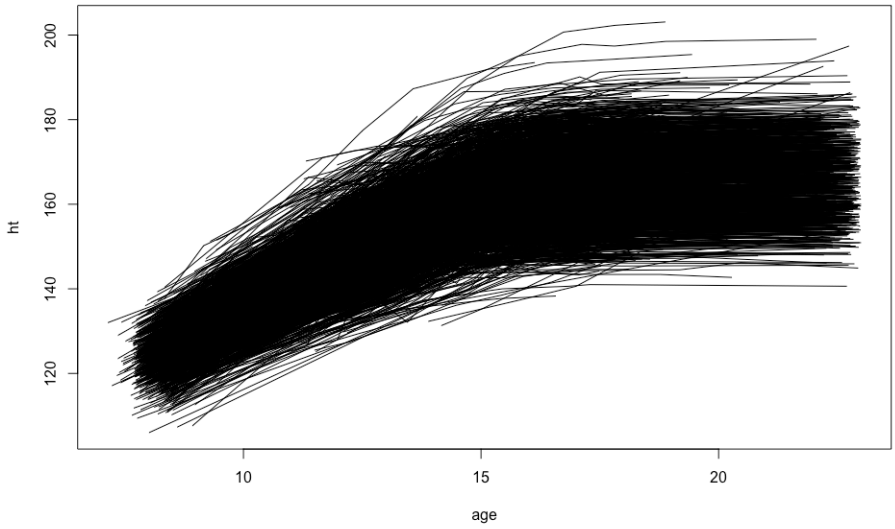

Figure 2-4: Outliers identified (a), highlighted (b) and cleaned (c) through the plotclean function in SITAR. The plot in panel B shows the values which have been highlighted as outliers and may be removed for the analyses.

2.5.2 Differences in the Prevalence

The Chi-square test was used to assess differences in the prevalence of undernutrition (stunting, underweight, and wasting) and overweight and obesity between sexes and races at each age group. However, in cases where the sample sizes were low, and more than 20% of the cells in the contingency table had expected values which were less than 5, the Fisher's exact test was used instead.

2.1.1 Generating Growth Centiles (Chapter 3)

The lambda mu sigma (LMS) method was used to generate growth percentiles. Model fit was determined using the Bayesian Information Criterion (BIC), with a lower BIC being preferred. Data were plotted for the 3rd, 50th and 97th centile for height, weight and BMI, the 10th, 50th and 90th centiles for waist circumference, and the 2.3rd, 50th and 97.7th centiles for hip circumference.

2.1.2 Modelling adolescent growth using SITAR (Chapter 4 & 5)

Data were modelled using the superimposition by translation and rotation (SITAR) growth curve model, a method based on mixed effects modelling. By fitting a spline model (B-spline), SITAR is able to fit a curve to all individual curves simultaneously and estimate individual variation using three random effects (corresponding to size, tempo and velocity):

$$y_{it} = \alpha_i + h\left(\frac{t - \beta_i}{e^{(-\gamma_i)}}\right) + \varepsilon_{it} \qquad 1$$

Where:

- y_{it} is height for subject i at time t
- h(t) is a natural cubic spline curve of height vs age
- α_i, β_i, γ_i are subject-specific random effects to make individual curves as similar as possible. These correspond to the parameters of pubertal growth, namely size, tempo and velocity. The interpretation of the random effects is explained in Cole et al (2010) and shown in the figure 3 below.

- ε_{it} is the residual error term with mean zero and constant variance

In this thesis, SITAR was used to assess racial differences and differences by pubertal status. Models were fitted for black and white children together using equation 1, and race was added for stratification as follows using white children as the reference:

$$y_{it} = \alpha_0 + \alpha_{white} + \alpha_i + h\left(\frac{t - \beta_0 - \beta_{white} - \beta_i}{e^{(-\gamma_0 - \gamma_{white} - \gamma_i)}}\right) + \varepsilon_{it} \qquad 2$$

The cubic spline function in fitted to all individuals simultaneously and the curves are adjusted for the random effects, choosing the values of α_i, β_i, γ_i (***Figure 2-5***) to "make individual growth curves as similar as possible" (230). The curve for SITAR is fitted to a shape-invariant model (230), which is based on a principle that the growth curves of individuals have a similar shape, despite their differences in size and growth rates. A shape-invariant models has been successfully applied by Beath in early childhood (231). Both the shape and the parameters of the function are estimated from the data, making them more biologically interpretable.

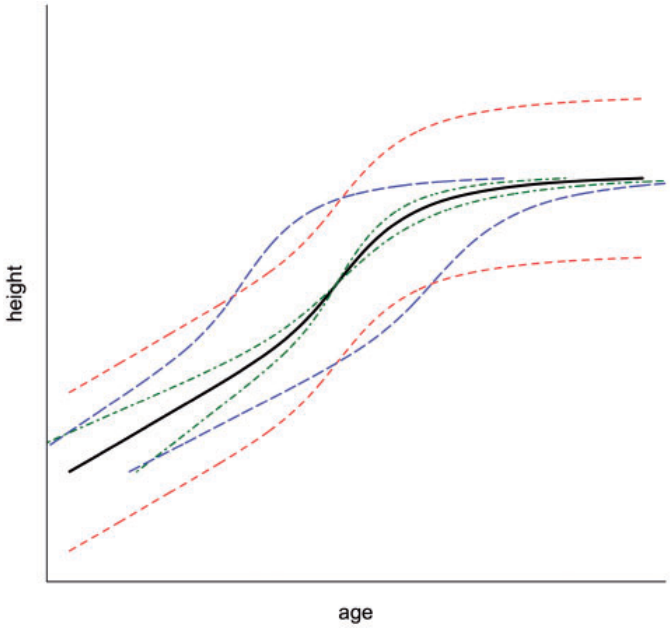

Figure 2-5: Plot to illustrate the three parameters of a SITAR model for height. The mean curve is represented by the solid black line. The three parameters are represented by the dashed lines as red (size or magnitude),blue (tempo or timing) and green (velocity or intensity). Source: Cole et al (230)

For this study, SITAR was chosen for its ability to handle missing data, and to model the growth of individuals with few data points. Given the long nature of this study, there was variation in the number of observations per participant, which would require imputation for some models. This was not required for SITAR. Additionally, the ability to capture individual growth variation to produce biologically interpretable random effects was an additional attraction to the model. Lastly, its versatility (wide application for modelling different dimensions and at different ages) made it easy to model different traits, and it is freely available in the R programming environment. Practically, SITAR was fitted by fitting different models in descending order of

degrees of freedom. The starting level for degrees of freedom was chosen as the integer that results from rounding down the mean number of observations for the sample, for a specific trait. For example, descriptive statistics of the number of observations for height are shown in

Table 2-1. The mean number of observations was 7.083 and the starting degrees of freedom was 7. Model fit was compared using the BIC and the model with the lowest BIC was chosen.

Table 2-1: Example of summary of number of observations for height

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
1.000	5.000	7.000	7.083	9.000	13.000

2.1.3 Regression analyses

Associations between early childhood growth and adolescent growth parameters as well as between adolescent growth and adult body composition were assessed using multiple linear regression analysis. To address the issue of collinearity, early life growth was defined using conditional growth measurements between birth and 24 months and between 24 and 60 months. All models were adjusted for maternal factors (age, education, parity) and SES, measured as sum of assets.

2.1.4 Assessing Patterns of Obesity and their effect on Linear Growth

The main results for this thesis are presented in chapters 3 to 5. However, additional results which are pertinent to the research question and to the hypotheses being tested in this thesis are presented in Chapter 6. These results complement the main results or address some of the questions raised in the empirical chapters of this thesis. The following analyses were performed:

2.1.5 Age-related Changes in Height Deficit and the Effect of Obesity on Linear Growth

Absolute deficit in height was determined by subtracting the age- and sex-specific median of the 2006 WHO child growth standards (3 to 60 months) and the 2007 WHO growth references (5 to 19 years) from the height of participant, matched for age in months. Means and standard errors were plotted for black and white males and females. Additionally, height deficit was determined by concurrent nutritional status (i.e., nutritional status at the specific age) and plotted for black children only, to test whether the deficit would be influenced by nutritional status.

2.1.6 Patterns of Obesity

The effect of the timing of onset overweight and obesity on the risk of adult obesity excess fat mass was investigated by generating four patterns which describe the period in which a participant first attained the status of overweight or obesity. Three periods were determined, birth to 8 years (childhood), 9 to 13 years (early adolescence) and 14 to 17 years (late adolescence). Adulthood was defined as the period from 18 to 24 years. Onset or presence was determined by at least one classification of overweight and obesity in a period. Four patterns were determined;

participants who never (N) became overweight or obese (O) in any period (pattern 1 – NNN), those who became overweight/obese in late adolescence (pattern 2 – NNO), those had onset in early adolescence through to late adolescence (pattern 3 – NOO), and lastly, those who had childhood onset through to late adolescence (pattern 4 – OOO). Using pattern 1 as the reference, the odds of becoming overweight or obese given any other pattern were determined using logistic regression.

Chapter 3 Patterns of Growth & Malnutrition

The prevalence of malnutrition and growth percentiles for urban South African children

Authors: Lukhanyo H. Nyati, John M. Pettifor, and Shane A. Norris

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Note: Due to document formatting (possibly the multiple section breaks), MS word has inserted a "0" between the chapter number and table or figure number in the legends. For example, Table 3-1 is labeled as Table 3-0-1. Correcting these manually removes the cross referencing, so they have not been corrected.

3.1 Abstract

Background

Low- and middle-income countries (LMIC) are experiencing a double-burden of malnutrition characterised by high prevalence of both under- and over-nutrition. We set out using data from the mixed-longitudinal Birth-to-Twenty Plus (Bt20+) birth cohort, to evaluate the patterns of malnutrition and growth in a large South African (SA) city by; (i) assessing the prevalence of undernutrition from birth to 5 years of age and overweight and obesity from ages 2 to 21 years in black and white, male and female children, and (ii) determining percentiles for height, weight, BMI, waist and hip circumferences and comparing the centiles to American and Dutch references.

Methods

Height, weight, waist and hip circumferences were measured on urban black and white SA children from the Bt20+. A total of 3273 children born between April and June 1990 in the Greater Johannesburg Metropolitan area were included in the cohort. Z-scores were derived using the WHO 2006 child growth standards (0–5 years), for defining stunting, underweight and wasting. The International Obesity Task Force (IOTF) references were used to define overweight and obesity. Percentiles were developed using the lambda mu sigma (LMS) method and compared to American and Dutch references.

Results

Black children were consistently shorter and black males lighter than white children and American references. The prevalence of stunting peaked at 2 years and was significantly higher in males than females and in black than white children. Black females had a greater prevalence of overweight and obesity than black males from 10 to 17 years. The percentiles for black females for weight and BMI were similar to those of South African white and American references but both black and white South African females had lower waist circumferences than American references.

Conclusion

The growth percentiles show that young South African urban black females are experiencing general but not central obesity due to a secular change which is faster in weight than height. High levels of undernutrition persist alongside high levels of over-nutrition with adolescence being a critical period for the upsurge in obesity in females. Early intervention is needed to combat the rise in obesity.

Keywords: stunting, wasting, overweight & obesity, growth references, South Africa

3.2 Background

Low-and middle income countries (LMIC) are experiencing a double-burden of malnutrition with an upsurge in overweight and obesity developing alongside persistently high levels of stunting (232). Globally, a three-fold increase in the prevalence of obesity has been observed since 1975, while in Africa, there has been a 50% increase in overweight in children under 5 years of age (8). The World Health Organisation (WHO) estimates that 15% of children aged 2 to 19 years globally are overweight or obese (7). Notwithstanding the rise in overweight and obesity, the prevalence of stunting remains persistently high, at about 40% in Africa, a level that has remained stagnant since 1990 and shows little prospect of improvement (4). The longitudinal assessment of growth and the social, economic, nutritional, behavioural and health environment in which it takes place can help identify critical periods associated with a rise in the prevalence of malnutrition and factors contributing to its development.

Bourne et al showed that since 1940, South Africa has been undergoing a nutrition transition with an increase in the contribution of fats and a decrease in the contribution of carbohydrates and fibre towards energy consumption (233). The transition is faster in the black than other populations (233) and in urban that rural populations (234), driving an upsurge in obesity in the black population. Historically, black children and adolescents of both sexes were shorter and lighter (183,185), and gained adipose tissue at a slower rate than white children (235). Previously, urban children from average socio-economic status (SES) communities were shorter and lighter than those in rural and well-off urban communities suggesting that a move to an urban environment without an improvement in SES does not benefit growth (99).

When compared with children from a high income country (HIC), South African children were historically shorter, lighter and had lower adipose tissue (55,236). More recently, data from the mixed-longitudinal Bt20+ cohort have shown that while South African urban children remain shorter and lighter than the National Centre for Health Statistics (NCHS) references, weight-for-height is greater or similar between birth and 5 years of age (219). Thus, while South African children continue to falter in linear growth, there is an indication of an early increase in adiposity. There is a need to study these patterns through childhood and adolescence and the mixed-longitudinal data from the Bt20+ cohort provides an opportunity to examine black and white urban children and to assess the changing patterns in obesity.

The current increase in obesity could be as a result of a general increase in obesity throughout the population or due to an increase within a subgroup of the population (237). Generating percentiles can demonstrate shifts in the centile lines over time to indicate whether the positive secular change in BMI is influenced by those in the upper centiles becoming heavier or an upward shift in all centiles. There are no percentiles for height, weight and BMI for South African children and thus it is not possible to assess the change in patterns that contribute to the secular trends in BMI. Thus, the aims of this study in urban South African children were; (i) to assess the prevalence of undernutrition from birth to 5 years of age and overweight and obesity from ages 2 to 21 years in black and white, male and female children, and (ii) to determine percentiles for height, weight, BMI, waist and hip circumferences and comparing the centiles to American and Dutch references.

3.3 Methods

Data for this study were obtained from the Birth to Twenty Plus study (Bt20+), a prospective longitudinal cohort of children born in the Greater Johannesburg region, South Africa. The majority of the black participants lived in Soweto, a "township" (underdeveloped suburban area) on the outskirts of the greater Johannesburg municipality, housing an estimated 40% of the close to 4 million people living in the city (214,215). Soweto was created in the early 1930s by the government which formalised the separation of residential areas for black and white citizens under the system of apartheid. The onset of this study coincided with the political changes leading to the end of apartheid.

Details of the cohort are described elsewhere but are briefly summarised here (216–218). The study enrolled children born during the seven weeks (217) between April 23 and June 8, 1990. Mothers with a permanent residential address in the municipal region were asked to participate in the study. Mothers were recruited at different time points, initially at antenatal clinics, then at delivery, and at 3 months, 6 months, and one year post-delivery (216). A total of 3273 mothers (black 78%, coloured 12%, Indian 4% & white 6%) with singleton births who met the selection criterion of continued residence in the area for 6 months were enrolled into the study (217). Due to the low number of white children in the original cohort, an additional number of white children born in the same period in 1990 were recruited at age 9 years. The government classification of population groups based on "race" was used (black for African, coloured for those of mixed ancestry, Indian for those whose forebears had immigrated from the Indian subcontinent and white for European-descent) and was assigned based on the parents' self-

reported racial classification. The black population in the Soweto-Johannesburg area is composed of different tribal groups identified by self-reported home language. Genetic variation among black participants had been previously assessed and showed that the cohort is largely homogeneous with a small contribution from diverse assortment of ancestral populations (223).

3.3.1 Anthropometric measurements

Weight was measured from birth while height was measured from 3 months to 24 years of age in black and white children. Waist and hip circumferences were measured from 9 to 24 years. Birth weight was obtained from health records; no data was available for birth length. Trained fieldworkers measured weight and length at 3, 6 and 12 months. From age 1 year, anthropometric measurements were collected on calendar year data collection cycles using standard methods (224,225). Between the birth and 8 years, height was measured using the method of Cameron (224), while from 10 years onwards all anthropometric measurements were done using the method of Lohman et al (225). The methods are similar and both advocate stretch height to reduce diurnal variation. All measurements up to data collection year 8 were done during home visits, while later measurements were done at the research centre. Before age 2 years, supine length was measured from the vertex of the head to the bottom of the heels, with the child lying flat on its back, head positioned in Frankfort vertical plane and knees straightened. After age 2 years, height was measured without shoes to the nearest 0.1 cm using a Harpenden Stadiometer (Holtain, U.K.). Weight was measured on an electronic scale to the nearest 0.1kg. Waist circumference was measured half way between the iliac crest and lowest rib at the end of normal expiration to the nearest 0.1 cm with no clothing barrier. Hip

circumferences was measured over the greater trochanter and the most protruding part of the buttocks to the nearest 0.1 cm with minimal clothing. Children with very low birth weight (< 1500g) were excluded from the estimation of undernutrition, given the likelihood of them having had a complicated postnatal course with respiratory, gastrointestinal and neurological complications, possibly leading to impaired growth during childhood. All participants (over the age of 11 years) and their guardians provided written informed assent and consent respectively and ethics approval was obtained from the University of the Witwatersrand Committee for Research on Human Subjects (M010556).

3.3.2 Generating growth percentiles

Growth percentiles were generated using the LMS function within the generalized additive models for location scale and shape (gamlss version 5.0-1) package in R (238,239). The LMS method summarizes the distribution of the data by age and sex in terms of three curves called lambda (L), mu (M) and sigma (S) (238). The M curve is the median by age, the S curve is the coefficient of variation, and the L curve expresses the skewness of the distribution in terms of the Box-Cox power needed to transform the data to near normality. Plots for the Bt20+ percentiles for height, weight and BMI were superimposed on plots for CDC growth references (240), while plots for the Bt20+ waist circumference references were superimposed on plots from the NHANES III (241). For height, weight and BMI, the 3rd, 50th and 97th centile are plotted while for waist circumference there being no centile lines below the 10th centile in the NHANES III data, the 10th, 50th and 90th centiles are presented. Plots for the Bt20+ hip circumference references were superimposed on Dutch references (242). Data for the Dutch references were

available for the -2, 0 and +2 standard deviation scores (SDS) corresponding to the 2.3rd, 50th and 97.7th centiles (242).

3.3.3 Generating Z-scores & BMI categories

The World Health Organization (WHO) 2006 child growth standards for children between birth and 5 years were used to develop height-for-age (HAZ), weight-for-age (WAZ), BMI-for-age (BMIZ) and weight-for-height (WHZ) Z-scores (67). Stunting, underweight and wasting were defined as a standard deviation score (SDS) < -2 of the median HAZ, WAZ and WHZ respectively. Overweight and obesity were defined using the International Obesity Task Force (IOTF) age-specific cut-offs for children aged 2 to 216 months (227). For children older than 216 months the adult cut-offs of BMI >= 25 & < 30 kg/m^2 and BMI >= 30 kg/m^2 were used to define overweight and obesity respectively.

3.3.4 Statistical analysis

Data were stratified into yearly age groups, which were defined as incorporating all children whose integer age was the same as the age group. For example, age group 1 included all children who had reached 1 year but were less than 2 years. Exceptions to the above definition were age group 'less than 1', which only included data for infants aged 3 months to less than 1 year and age group '21', which included all participants aged 21 years and above. Data were analysed using R version 3.3.1 and Stata version 13.1 (Stata-Corp LP, College Station, Texas, USA). Z-scores were generated using the WHO 2006 and WHO 2007 R macros (243,244). The

programme automatically generates variables, flagging biologically implausible values. These latter values were excluded from the analyses. Additional cleaning to remove outliers was achieved using the plotclean function in the SITAR package (version 1.0.9) in R (230).
Race and sex differences in the proportions of stunting, underweight, wasting, overweight and obesity were assessed using a Pearson Chi-squared test. Race differences in height, weight and BMI were assessed using an independent t-test. All tests were performed at the 5% significance level.

3.4 Results

3.4.1 Race differences in height, weight, BMI, waist and hip circumference and waist-to-height ratio

The number of participants in each age group of the Bt20+ are presented in table 1a. As the cohort represented the demographics of children in Soweto-Johannesburg, South Africa, a higher number of black than white children were enrolled in the study. Cross-sectional means of height, weight, BMI, waist and hip circumferences and waist-to-height ratio are presented in ***Table 3-0-1***. With the exception of age less than 1 year and mid-childhood (5 and 8 years of age), white children were consistently taller than black children from early childhood to young adulthood. The earliest significant race differences were observed at 1 year in males and at 2 years in females such that the mean difference increased from 3.7 cm at 1 year to 7.9 cm at 19 years in males ($p < 0.0001$) while in females the mean difference changed from 4.3 cm at 2 years to 5.2 cm at 19 years ($p < 0.0001$).

Table 3-0-1: Race differences in (a) height/length, (b) weight, (c) BMI, (d) waist circumference, (e) hip circumference, and (f) waist-to-height ratio (%) from birth to adulthood. Sample sizes are given in table 1(a) in square brackets. Length was not measured at birth.

(a) Height

Age group	Males Mean + SD (cm) [N]			Females Mean + SD (cm) [N]		
	Black	White	P-value	Black	White	P-value
Birth	NA	NA	NA	NA	NA	NA
< 1	67.8 (6.9) [417]	67.1 (7.0) [66]	0.39	66.6 (6.8) [423]	66.2 (6.9) [48]	0.708
1	77.0 (4.7) [376]	80.7 (4.7) [23]	**0.001**	75.8 (4.7) [422]	77.8 (5.2) [24]	0.085
2	83.4 (3.6) [296]	87.8 (4.8) [31]	**<0.0001**	82.6 (3.8) [300]	86.9 (3.9) [24]	**<0.0001**
5	100.5 (4.0) [519]	104.5 (6.2) [18]	0.382	100.4 (4.3) [560]	102.5 (2.8) [17]	0.22
8	125.4 (6.1) [372]	125.1 (6.7) [15]	0.881	124.6 (5.9) [407]	126.1 (4.5) [12]	0.283
9	132.1 (5.9) [251]	137.1 (5.9) [42]	**<0.0001**	132.8 (5.6) [253]	136.0 (6.6) [39]	**0.005**
10	137.4 (6.2) [182]	143.3 (7.2) [73]	**<0.0001**	139.2 (6.3) [159]	142.9 (7.5) [65]	**0.001**
11	142.8 (6.7) [470]	148.7 (7.7) [73]	**<0.0001**	145.8 (7.4) [505]	148.3 (8.0) [69]	**0.018**
12	147.6 (7.5) [603]	155.8 (9.0) [72]	**<0.0001**	151.4 (6.8) [685]	155.0 (7.9) [78]	**<0.0001**
13	153.8 (8.3) [613]	164.0 (9.9) [57]	**<0.0001**	155.5 (6.2) [690]	160.3 (6.7) [63]	**<0.0001**
14	160.2 (8.4) [701]	169.8 (9.1) [58]	**<0.0001**	157.3 (5.9) [754]	162.9 (6.8) [74]	**<0.0001**
15	165.6 (7.8) [759]	174.8 (8.4) [58]	**<0.0001**	158.4 (6.2) [841]	163.8 (6.9) [61]	**<0.0001**
16	168.6 (7.1) [685]	176.6 (7.8) [53]	**<0.0001**	158.8 (5.9) [724]	164.5 (6.6) [61]	**<0.0001**
17	170.3 (6.7) [502]	177.7 (8.8) [48]	**<0.0001**	159.3 (6.2) [561]	165.3 (6.8) [61]	**<0.0001**
18	171.2 (6.6) [449]	178.0 (8.0) [37]	**<0.0001**	159.4 (6.1) [427]	166.3 (7.1) [36]	**<0.0001**
19	170.0 (6.8) [55]	177.9 (7.7) [40]	**<0.0001**	158.9 (6.5) [47]	164.1 (6.9) [42]	**<0.0001**
20	171.3 (6.9) [103]	174.3 (6.8) [12]	0.183	158.8 (5.9) [99]	164.5 (6.7) [7]	0.066
21	171.6 (6.6) [695]	178.4 (7.4) [17]	**0.002**	159.7 (6.1) [711]	166.2 (7.2) [23]	**<0.0001**

(b) Weight

Age group	Males Mean + SD (kg)			Females Mean + SD (kg)		
	Black	White	P-value	Black	White	P-value
Birth	3.1 (0.5)	3.3 (0.5)	**0.019**	3.0 (0.5)	3.1 (0.5)	0.098
< 1	8.3 (1.9)	7.6 (2.0)	0.083	7.8 (1.7)	7.3 (2.0)	0.098
1	10.5 (1.7)	11.0 (1.7)	0.158	10.1 (1.7)	10.2 (2.0)	0.738
2	11.5 (1.7)	13.0 (1.6)	**<0.0001**	11.4 (1.6)	12.0 (1.4)	**0.037**
5	16.0 (2.0)	16.5 (2.9)	0.814	15.8 (2.1)	16.4 (0.7)	0.188
8	25.2 (3.9)	28.1 (9.2)	0.228	24.9 (4.7)	26.1 (3.7)	0.312
9	28.8 (5.0)	32.7 (7.4)	**0.023**	29.6 (6.4)	30.3 (6.3)	0.541
10	32.6 (6.6)	35.6 (6.2)	**0.009**	34.7 (8.3)	36.1 (8.1)	0.248

11	35.7 (8.0)	39.8 (7.3)	**<0.0001**	38.9 (10.0)	40.5 (9.4)	0.189
12	39.5 (8.6)	45.6 (10.3)	**<0.0001**	44.8 (10.9)	46.4 (11.0)	0.244
13	44.1 (9.9)	53.2 (12.1)	**<0.0001**	50.1 (11.9)	51.8 (10.9)	0.228
14	49.2 (10.6)	59.4 (12.8)	**<0.0001**	53.2 (11.5)	55.5 (10.9)	0.094
15	53.8 (10.4)	64.9 (12.6)	**<0.0001**	55.7 (11.7)	57.0 (10.1)	0.343
16	56.9 (9.9)	66.7 (10.8)	**<0.0001**	57.6 (12.1)	59.2 (10.6)	0.276
17	59.0 (9.8)	71.3 (12.2)	**<0.0001**	59.0 (11.5)	60.1 (12.3)	0.494
18	59.8 (9.7)	71.1 (12.9)	**<0.0001**	59.1 (11.9)	63.1 (12.9)	0.079
19	63.1 (14.5)	73.9 (16.5)	**0.013**	61.4 (13.8)	61.9 (15.2)	0.881
20	62.5 (11.0)	68.6 (8.1)	**0.033**	60.4 (12.8)	69.8 (9.4)	**0.039**
21	63.6 (11.6)	75.1 (10.7)	**0.004**	65.1 (16.1)	59.9 (10.2)	**0.027**

(c) BMI

Age group	Males Mean + SD (kg/m^2)			Females Mean + SD (kg/m^2)		
	Black	White	P-value	Black	White	P-value
Birth	NA	NA	NA	NA	NA	NA
< 1	17.9 (2.3)	16.7 (1.6)	**<0.0001**	17.5 (2.0)	16.2 (1.9)	**0.001**
1	17.7 (1.8)	16.9 (1.7)	**0.044**	17.5 (1.9)	16.7 (1.6)	**0.041**
2	16.5 (2.2)	16.9 (1.6)	0.197	16.7 (2.0)	15.9 (1.8)	0.067
5	15.8 (1.3)	15.0 (0.9)	0.259	15.6 (1.3)	15.6 (0.6)	0.990
8	15.9 (1.5)	17.7 (4.5)	0.146	16.0 (2.1)	16.4 (2.0)	0.509
9	16.4 (2.0)	17.3 (3.1)	0.105	16.7 (2.8)	16.2 (2.1)	0.224
10	17.2 (2.6)	17.3 (2.1)	0.875	17.8 (3.4)	17.5 (2.6)	0.522
11	17.4 (3.1)	18.0 (2.5)	0.099	18.2 (3.8)	18.3 (2.9)	0.866
12	18.0 (2.9)	18.7 (3.3)	0.111	19.4 (4.0)	19.1 (3.2)	0.366
13	18.5 (3.2)	19.6 (3.2)	**0.018**	20.6 (4.4)	20.0 (3.4)	0.186
14	19.1 (3.3)	20.5 (3.5)	**0.039**	21.4 (4.3)	20.8 (3.6)	0.179
15	19.6 (3.1)	21.2 (3.4)	**0.009**	22.2 (4.4)	21.2 (3.4)	**0.042**
16	20.0 (3.0)	21.3 (2.7)	**0.013**	22.8 (4.5)	21.8 (3.3)	**0.027**
17	20.3 (3.0)	22.5 (3.1)	**<0.0001**	23.2 (4.4)	21.9 (4.0)	**0.019**
18	20.4 (2.8)	22.4 (3.6)	**0.017**	23.2 (4.4)	22.8 (3.9)	0.490
19	21.8 (5.1)	23.3 (5.0)	0.168	24.3 (5.0)	22.9 (4.8)	0.178
20	21.3 (3.3)	22.6 (2.8)	0.146	23.9 (4.7)	25.8 (2.7)	0.142
21	21.6 (3.7)	23.5 (2.4)	0.055	25.5 (6.1)	21.7 (3.9)	**0.001**

(d) Waist circumference

Age group	Males Mean + SD (cm)			Females Mean + SD (cm)		
	Black	White	P-value	Black	White	P-value
9	57.1 (4.9)	59.9 (8.1)	**0.046**	57.2 (6.5)	57.7 (5.9)	0.648
10	58.7 (5.8)	60.8 (5.6)	**0.008**	58.4 (6.9)	59.5 (7.0)	0.277
11	60.6 (6.8)	63.4 (6.6)	**0.001**	61.4 (7.5)	63.0 (8.7)	0.167
12	62.6 (6.9)	66.1 (7.2)	**<0.0001**	63.8 (7.8)	65.3 (8.4)	0.154
13	64.7 (7.5)	69.3 (7.8)	**<0.0001**	67.3 (9.0)	67.7 (7.8)	0.709
14	67.0 (7.6)	72.1 (8.8)	**<0.0001**	69.3 (9.1)	69.1 (8.5)	0.814
15	69.1 (7.8)	73.7 (9.6)	**<0.0001**	71.0 (9.6)	69.6 (8.7)	0.233
16	69.4 (6.5)	75.6 (7.1)	**<0.0001**	71.9 (9.8)	73.7 (9.4)	0.146
17	71.3 (7.2)	77.7 (7.4)	**<0.0001**	74.3 (9.8)	74.8 (10.4)	0.701

18	72.6 (7.0)	77.1 (5.4)	**0.002**	76.0 (11.3)	78.2 (11.7)	0.396
19	73.3 (11.3)	81.7 (14.6)	**0.021**	72.7 (10.2)	67.9 (6.4)	**0.022**
20	71.7 (7.6)	76.7 (6.0)	**0.020**	69.3 (8.2)	76.4 (8.8)	0.080
21	75.7 (9.1)	82.9 (6.8)	**<0.0001**	81.1 (13.2)	72.4 (9.3)	**<0.0001**

(e) Hip circumference

Age group	Males Mean + SD (cm)			Females Mean + SD (cm)		
	Black	White	P-value	Black	White	P-value
9	63.4 (6.2)	66.3 (8.2)	**0.044**	65.8 (9.3)	66.3 (7.4)	0.746
10	71.0 (6.8)	73.7 (6.6)	**0.004**	75.1 (8.9)	75.6 (7.5)	0.670
11	76.4 (8.0)	78.0 (6.7)	0.088	80.3 (9.6)	79.0 (7.8)	0.201
12	78.6 (8.1)	81.5 (7.9)	**0.004**	85.2 (10.2)	84.6 (9.4)	0.635
13	81.5 (8.9)	86.2 (8.6)	**<0.0001**	90.9 (10.4)	90.4 (8.9)	0.673
14	84.4 (8.4)	89.8 (8.6)	**<0.0001**	94.3 (10.0)	92.6 (8.1)	0.079
15	87.5 (8.4)	92.5 (9.7)	**<0.0001**	95.7 (10.0)	94.4 (7.2)	0.193
16	89.3 (7.4)	92.8 (7.2)	**0.001**	96.8 (9.6)	95.5 (8.5)	0.221
17	90.8 (7.8)	94.0 (7.0)	**0.002**	99.5 (9.5)	95.2 (8.3)	**<0.0001**
18	90.8 (6.9)	92.5 (5.6)	0.196	99.4 (10.2)	97.6 (8.2)	0.339
19	90.7 (10.5)	97.1 (11.0)	**0.027**	100.0 (11.9)	93.8 (8.4)	**0.020**
20	90.8 (7.6)	95.0 (6.9)	0.075	98.6 (10.9)	101.1 (6.4)	0.378
21	93.3 (8.5)	99.1 (6.0)	**0.001**	104.6 (12.9)	96.1 (8.8)	**<0.0001**

(f) Waist-to-height ratio

Age group	Males Mean + SD			Females Mean + SD		
	Black	White	P-value	Black	White	P-value
9	43.0 (3.3)	43.6 (5.3)	0.514	42.8 (4.0)	42.3 (3.3)	0.458
10	42.7 (3.8)	42.4 (3.2)	0.510	42.0 (4.3)	41.6 (4.0)	0.596
11	42.4 (4.2)	42.8 (4.4)	0.508	42.1 (4.6)	42.4 (4.8)	0.601
12	42.4 (4.0)	42.4 (4.2)	0.912	42.1 (4.9)	42.1 (4.8)	0.888
13	42.1 (4.6)	42.3 (4.2)	0.777	43.3 (5.7)	42.2 (4.3)	0.057
14	41.8 (4.7)	42.5 (5.0)	0.327	44.0 (5.7)	42.6 (5.1)	**0.021**
15	41.7 (4.7)	41.8 (4.2)	0.843	44.8 (6.0)	42.6 (5.3)	**0.003**
16	41.2 (3.8)	42.8 (3.6)	**0.002**	45.3 (6.3)	44.7 (5.3)	0.418
17	41.8 (4.2)	43.8 (3.8)	**0.001**	46.7 (6.3)	45.4 (6.2)	0.097
18	42.4 (3.9)	43.6 (3.0)	0.082	47.6 (6.9)	47.5 (6.3)	0.935
19	43.2 (7.0)	46.2 (8.4)	0.150	45.8 (6.4)	41.3 (3.6)	**0.001**
20	41.9 (4.4)	44.1 (4.1)	0.110	43.7 (5.2)	46.4 (4.6)	0.181
21	44.2 (5.3)	46.5 (3.2)	**0.009**	50.8 (8.3)	43.6 (5.6)	**<0.0001**

Age group < 1 = age between 3 months and 1 year; 21 = age 21 years or greater

Similarly for weight, white males, who were 200g heavier at birth ($p = 0.019$), were consistently heavier than black males except in infancy and mid-childhood. Mean differences increased from 2.5 kg ($p < 0.001$) to 10.8 kg ($p = 0.013$) between ages 2 and 19 years. In females, there were no

consistent differences in weight between black and white participants. BMI was greater in black than white infants during the first two years of life. The reverse was observed in males during adolescence (white males having significantly greater BMI than black males between 13 and 18 years). Black females had significantly greater BMI than white females from ages 15 to 17 years.

White males had greater waist and hip circumferences than black males at most ages except at 11, 18 and 19 years for hip circumference. Waist-to-height ratios were similar in black and white males except at ages 16, 17 and 21 years when white males had greater waist-to-height ratio than black males. In females, there were no race differences in waist and hip circumferences except at ages 19 and 21 years for waist circumference, and at ages 17, 19 and 21 years for hip circumference. Black females had greater waist-to-height ratio than white females at ages 14, 15, 19 and 21 years.

3.4.2 Patterns of malnutrition

The prevalence of stunting, underweight and wasting from birth to 5 years, and overweight and obesity from 2 to 21+ years are presented in ***Figure 3-0-1*** and ***Table 3-0-2***. Black children were more stunted than white children at all ages up to and including the 5-year age group, and males were more stunted than females except in the 5-year age group. Stunting reached a peak of 34% and 25% in black males and females at 2 years respectively. Black males tended to be more underweight than black females during the first three years of life, while there were no consistent patterns between the race groups in the first 5 years. The prevalence of wasting was low at all

times in the first three years, although black males in the 2-year age group had a higher prevalence than the other three groups

Table 3-0-2: Ethnic and sex differences in the prevalence of (a) stunting, (b) underweight, (c) wasting, and (d) overweight and obesity. Sex differences are indicated by asterisks

(a) Stunting

Age group	Black boys		White boys		P-value	Black girls		White girls		P-value
	n	freq (%)	n	freq (%)		n	freq (%)	n	freq (%)	
< 1	588	118 (20.1)**	99	5 (5.1)	**<0.0001**	582	81 (13.9)	79	1 (1.3)	**0.001**
1	423	88 (20.8)	24	2 (8.3)	0.138	467	80 (17.1)	25	3 (12.0)	0.505
2	299	103 (34.4)*	30	5 (16.7)*	**0.048**	305	76 (24.9)	24	0 (0.0)	**<0.0001**
5	519	38 (7.3)	18	0 (0.0)	0.234	561	37 (6.6)	17	0 (0.0)	0.274

(b) Underweight

Age group	Black boys		White boys		P-value	Black girls		White girls		P-value
	n	freq (%)	n	freq (%)		n	freq (%)	n	freq (%)	
birth	1245	112 (9.0)	152	7 (4.6)	0.067	1324	110 (8.3)	148	11 (7.4)	0.713
< 1	591	38 (6.4)**	96	6 (6.3)	0.947	580	15 (2.6)	77	2 (2.6)	0.995
1	402	19 (4.7)**	24	2 (8.3)	0.428	441	7 (1.6)	25	2 (8.0)	**0.023**
2	300	42 (14.0)**	31	0 (0.0)	**0.026**	304	20 (6.6)	24	0 (0.0)	0.195
5	519	12 (2.3)	18	1 (5.6)	0.379	561	18 (3.2)	17	0 (0.0)	0.532

(c) Wasting

Age group	Black boys		White boys		P-value	Black girls		White girls		P-value
	n	freq (%)	n	freq (%)		n	freq (%)	n	freq (%)	
< 1	588	26 (4.4)	95	4 (4.2)	0.926	580	15 (2.6)	76	5 (6.6)	0.057
1	398	7 (1.8)	24	1 (4.2)	0.401	439	4 (0.9)	25	1 (4.0)	0.146
2	299	28 (9.4)	30	0 (0.0)	**0.030**	303	16 (5.3)	24	1 (4.2)	0.813

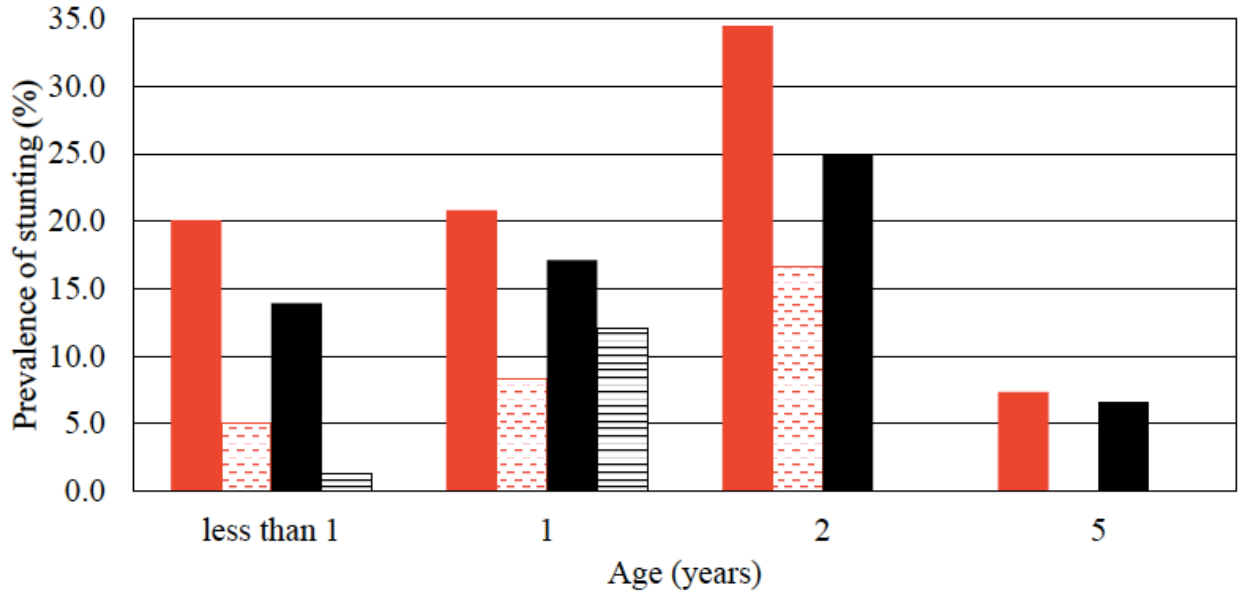
(d) Overweight & obesity

Age group	Black boys		White boys		P-value	Black girls		White girls		P-value
	n	freq (%)	n	freq (%)		n	freq (%)	n	freq (%)	
2	298	65 (21.8)	30	4 (13.3)	0.277	299	71 (23.7)	24	3 (12.5)	0.207
5	519	55 (10.6)	18	1 (5.6)	0.491	560	61 (10.9)	17	2 (11.8)	0.901
9	255	19 (7.5)*	43	5 (11.6)	0.352	253	36 (14.2)	41	5 (12.2)	0.727
10	183	19 (10.4)	73	7 (9.6)	0.850	159	26 (16.4)	65	13 (20.0)	0.513
11	472	47 (10.0)*	73	9 (12.3)	0.535	506	77 (15.2)	69	13 (18.8)	0.437
12	616	68 (11.0)***	72	6 (8.3)*	0.483	702	133 (18.9)	79	17 (21.5)	0.582
13	643	62 (9.6)***	57	8 (14.0)	0.289	726	153 (21.1)	63	11 (17.5)	0.498
14	767	67 (8.7)***	60	10 (16.7)	0.042	809	174 (21.5)	75	12 (16.0)	0.263
15	803	66 (8.2)***	61	9 (14.8)	0.081	886	224 (25.3)	62	9 (14.5)	0.057
16	722	51 (7.1)***	61	6 (9.8)	0.424	749	206 (27.5)	65	12 (18.5)	0.114
17	581	44 (7.6)***	55	14 (25.5)	**<0.001**	645	190 (29.5)	70	12 (17.1)	**0.030**
18	452	29 (6.4)***	38	7 (18.4)	**0.016**	433	114 (26.3)	36	9 (25.0)	1.000
19	55	6 (10.9)**	40	10 (25.0)	0.125	47	17 (36.2)	42	11 (26.2)	0.433
21+	756	113 (14.9)***	17	5 (29.4)	0.194	748	348 (46.5)	23	6 (26.1)	0.085

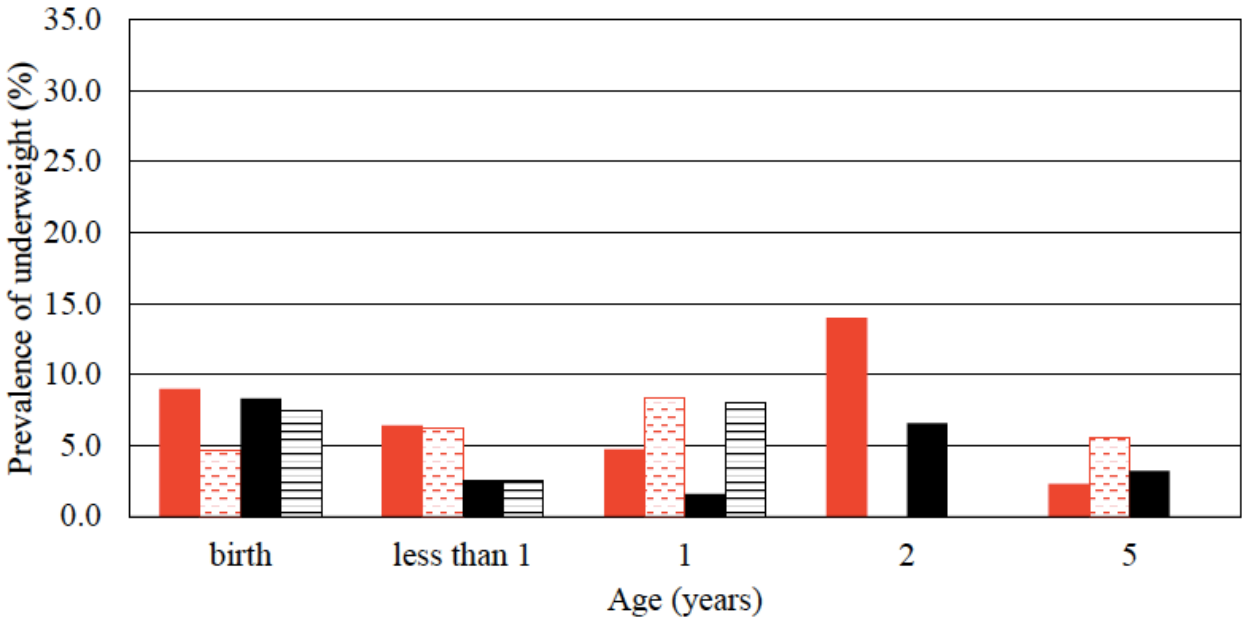
Age group < 1 = age between 3 months and 1 year; *p < 0.05; **p < 0.01, ***p < 0.001

In both race and sex groups, the prevalence of overweight and obesity was high in the 2-year age group, but the prevalence then fell in all groups. In black males, the prevalence changed little from age 5 years onwards, remaining below 10% at most time points, reaching a peak of 14.9% at 21+ years. The prevalence in white males was consistently higher than that in black males after 12 years of age and rose sharply to 29.4% in the 21+ years age group. Females of both race groups had a higher prevalence of overweight and obesity than males throughout childhood and the adolescent period, with black females having a steady rise in prevalence from 11 years of age, reaching 46.5% in the 21+ years age group. The prevalence in white females changed little from 10 years of age, remaining between 15 and 20% throughout adolescence.

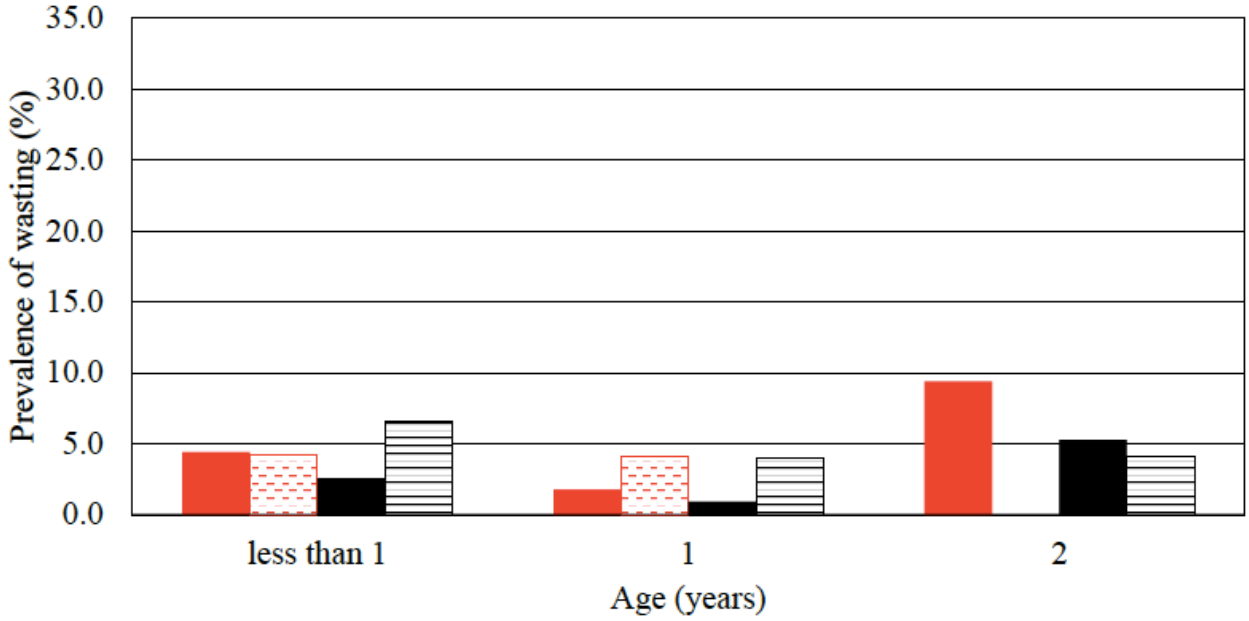
(a)


35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Prevalence of stunting (%)
less than 1
1
2
5
Age (years)

(b)


35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Prevalence of underweight (%)
birth
less than 1
1
2
5
Age (years)

(c)



(d)

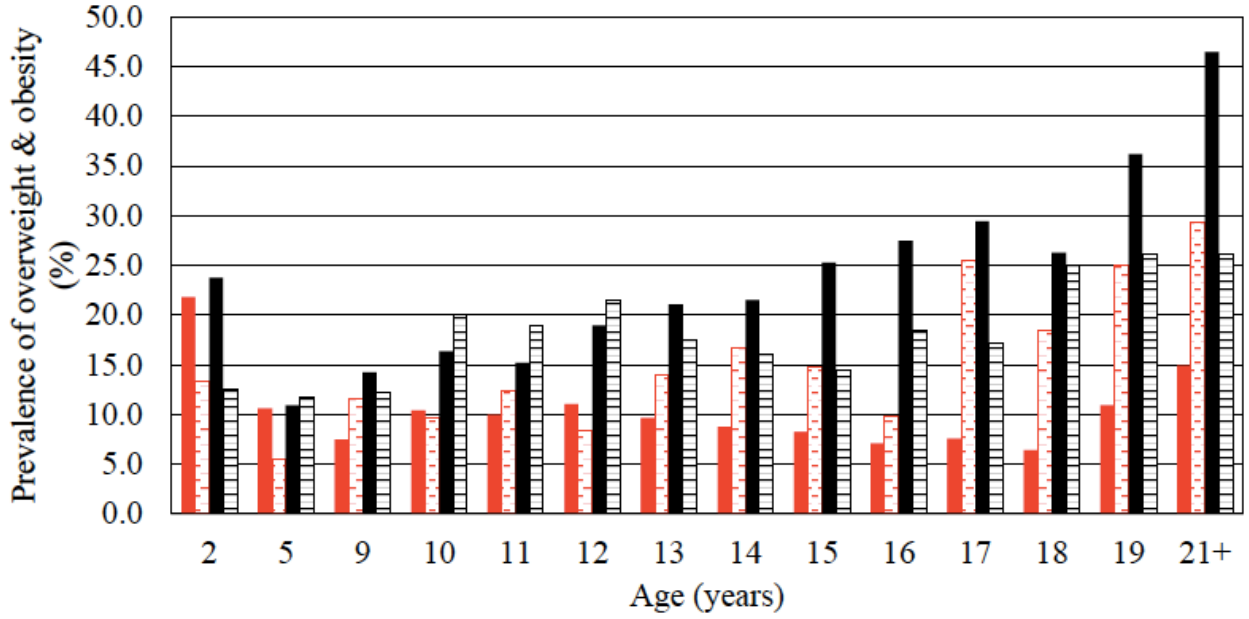


Figure 3-0-1: Prevalence of (a) stunting (b) underweight (c) wasting (d) overweight and obesity for black boys (red solid), white boys (red dashed), black girls (black solid), and white girls (black lines)

3.4.3 Height, weight, BMI, waist and hip circumference percentiles

Values for the 3rd, 50th, and 97th centiles for height, weight and BMI from age 2 to 20 years, 10th, 50th and 90th centiles for waist circumferences and 2.3rd, 50th and 97.7th centiles for hip circumference from 9 to 18 years are given in ***Table 3-0-3***. The Bt20+ centile lines for black and white children were superimposed on the 2000 CDC growth charts for height, weight and BMI, on NHANES III reference charts for waist circumference and Dutch references for hip circumferences (***Figure 3-0-2***). The weight, height and BMI centiles for white Bt20+ children were similar to those of the 2000 CDC charts. However, for black children, height centile lines were lower than those of both the 2000 CDC charts and Bt20+ white children, such that the 50th centile of the black children corresponded to the 25th of the 2000 CDC growth charts for both sexes. A similar pattern was observed for weight and BMI centile lines for black males, but differed for black females, whose lines were similar to the 2000 CDC charts and those of Bt20+ white females.

The centile lines for waist circumferences for Bt20+ children of both sexes were lower than the NHANES III. During adolescence, the 90th centile of Bt20+ black and white males was just above the 50th centile of the American males. While the 50th centile of Bt20+ white males was below the NHANES III males, the 10th centile for Bt20+ white and NHANES III males were similar. Bt20+ black and white females showed similar patterns and were lower than the NHANES III females. The bands of NHANES III appeared wider than those of the Bt20+ sample. For hip circumference, centile lines for black children showed an acceleration between 9

and 11 years from lower centiles approaching centiles of white children between 10 and 11 years. The 2.3rd centile of Bt20+ black and white females were higher than that of Dutch females. Bt20+ black and white girls showed similar patterns except for the 97.7th centile, which were higher in black than white females.

3.5 Discussion

We assessed the prevalence of malnutrition among a population of urban South African children and generated percentile values for children living in the Johannesburg metropolitan region. Between birth and 5 years, the prevalence of stunting was higher in black than white children and in males than females reaching a peak at 2 years of age at over 34% for black males. This is higher than the national average of 26% for children from birth to 3 years (13) and remarkably higher than the 6% average for children from birth to 5 years from HIC (4). Micronutrient deficiency in early childhood may be responsible for the high rate of undernutrition in black children (13). On the contrary, the prevalence of overweight and obesity of South African females were comparable to those of American females who had an average of 26.5 and 41.9 % for non-Hispanic white and African American females respectively between 12 and 19 years of age (245). In our sample, the prevalence of overweight and obesity ranged from about 19 to 36% and from about 22 to 26% between 12 and 19 years of age for black and white females respectively. In adulthood, black women have a higher prevalence of obesity than white women while the prevalence of overweight is similar between the two groups (107).

The rise in the prevalence of overweight and obesity may be attributed to poor dietary patterns and low levels of physical activity among black children. Black children of both sexes in the Bt20+ cohort had significantly lower levels of reported physical activity than white children (246). Additionally, among Bt20+ black children, dietary patterns differed with a greater proportion of females consuming snacks and confectionary and a lower proportion taking lunchboxes to school than males, contributing to possibly higher consumption of fats and refined sugar (247). Residential mobility among those experiencing an increase in SES between birth and 15 years of age was associated with a greater BMI in females, but not in males. Thus, the socio-economic transition may predispose females to greater exposure to bad dietary practices both within and without the household, while maintaining similarly low levels of physical activity compared to males.

Changing dietary patterns could be driving a positive secular change in BMI such that the centiles for black females are now similar to those of white South African females and American references. Historically, black females had lower weight and adiposity than white females (183,235). Compared to two nationally representative references of American children, the weight and BMI centiles for Bt20+ females are similar to American references for all centiles. There are no historical growth reference data to assess whether the secular change in BMI is affecting all centiles and thus it is unclear whether in South Africa, the rise in BMI affects those in a select group or affect all centiles. In America, the rise in obesity was driven by the heaviest sub-group (> 95^{th} centile) being much heavier than the same group in previous surveys, while the lower centiles were similar for children and adolescents between surveys, leading to a widening of the upper centiles (237). For waist circumference, South African females started lower but

grew towards the American references in adolescence. This suggests that the pattern of obesity of younger South African females differs from that of American peers, with general rather than abdominal obesity among South African children.

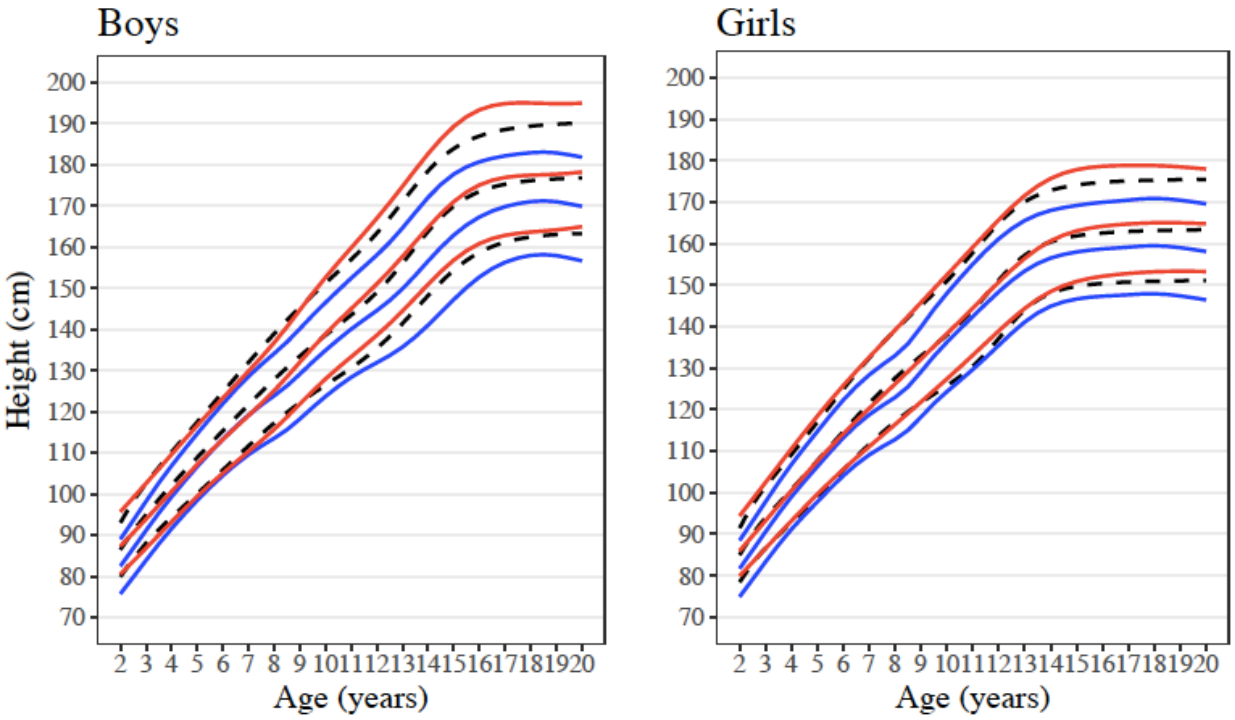
The percentiles produced in this study will be useful for future comparisons to assess patterns in the secular changes in weight and BMI so as to give insight into factors that drive the obesity epidemic. Nevertheless, this study has several limitations in that the data are not nationally representative and external validity of the Bt20+ sample was only conducted at birth. There were no differences in maternal age, gravidity and birth weight between Bt20+ participants and those born in the same year but outside of the 7 week recruitment period for the cohort (216). The Soweto-Johannesburg Metropolitan area has experienced significant inward migration and children who recently migrated into this area are significantly more disadvantaged compared to long-term residents (102), thus these percentiles are representative of children born in Soweto in the early 90's who have had long-term residence in the township. A second limitation of the study is the relatively small number of white children, particularly in early life, even though the proportions represent the demographics of population at the time of birth.

3.6 Conclusions

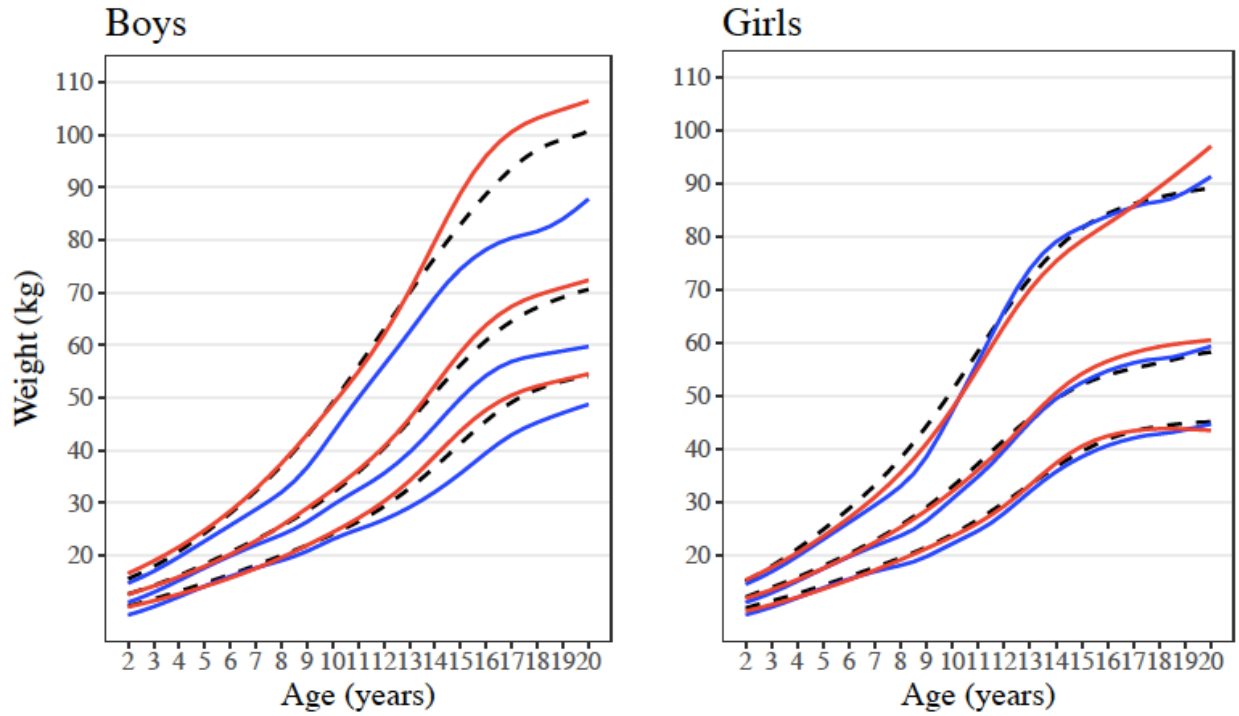
In conclusion, the availability of data describing growth patterns is a critical tool for current and future comparisons and is essential for public health. More studies are needed to establish whether the positive secular change in weight and BMI affects the general population or a sub-group. This would assist with developing a targeted intervention against obesity. The risk for

overweight and obesity in South African females increases in early adolescence, and may be linked to early life growth and physiological and lifestyle changes during that period. Early intervention is needed in females to mitigate against the upsurge of overweight and obesity.

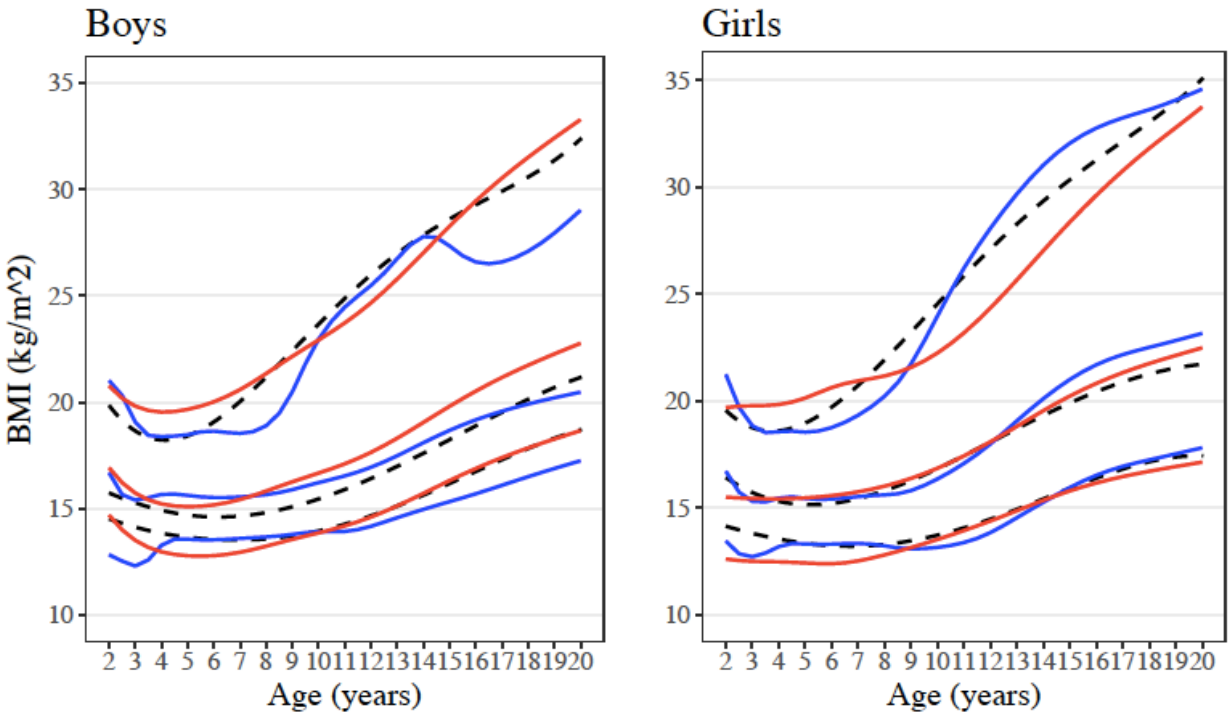
(a)


Boys
Girls
Height (cm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age (years)

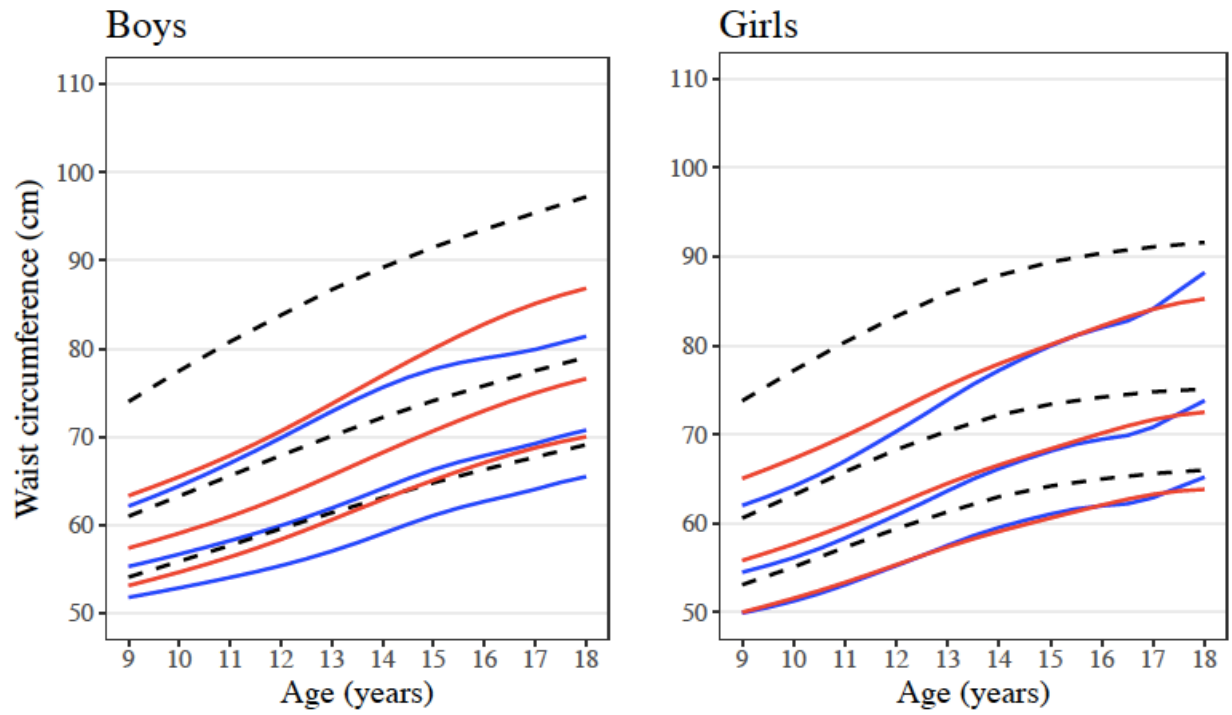
(b)


Boys
Girls
Weight (kg)
110
100
90
80
70
60
50
40
30
20
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age (years)

(c)


Boys
Girls
BMI (kg/m^2)
35
30
25
20
15
10
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age (years)

(d)


Boys
Girls
Waist circumference (cm)
110
100
90
80
70
60
50
9 10 11 12 13 14 15 16 17 18
Age (years)

(e)

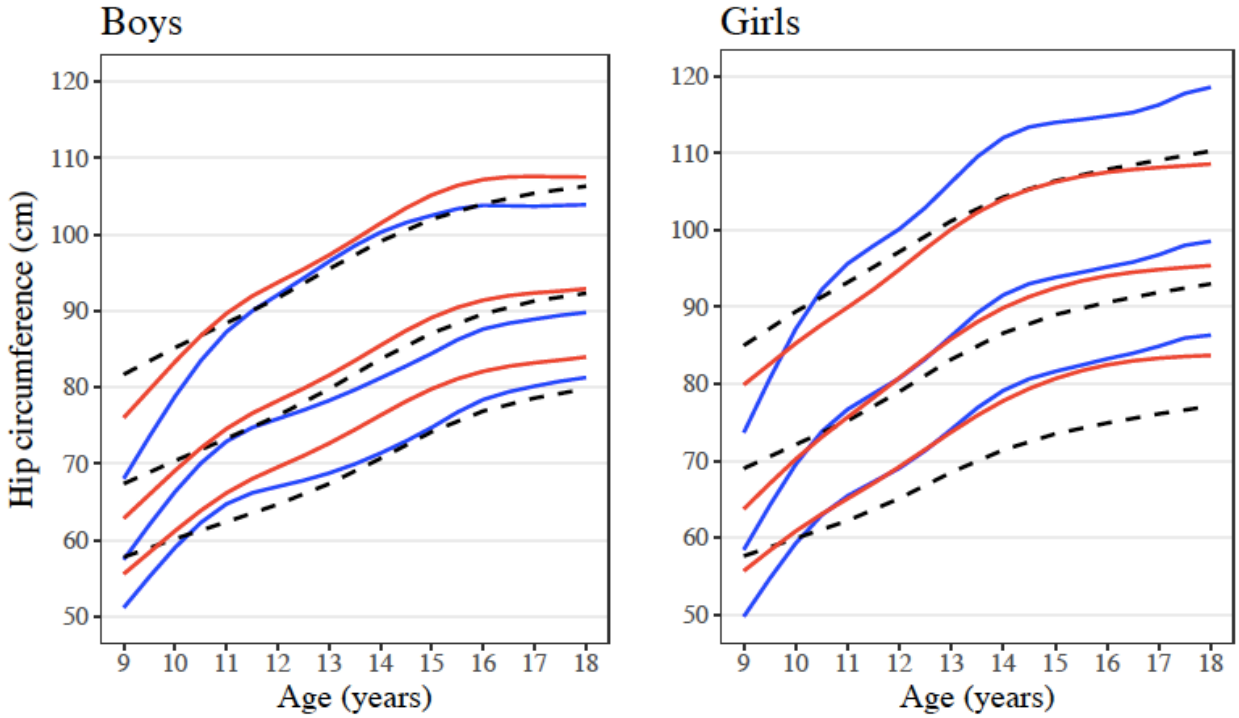


Figure 3-0-2: Comparison of centile lines (3, 50, 97 for height, weight & BMI, 10, 50, 90 for waist circumference, and 2.3rd, 50th & 97.7th for hip circumference) between South African black (blue), white (red) children for (a) height, (b) weight, and (c) BMI compared to CDC references (black-dashed), (d) waist circumference compared to NHANES III references (black-dashed), and (e) hip circumference compared to Dutch references (black-dashed)

Table 3-0-3: Percentile values for the 3rd, 50th, and 97th centiles for (a) height, (b) weight, (c) BMI, (d), 10th, 50th and 90th centiles for waist circumference, and (e) 2.3rd, 50th and 97.7th for hip circumference

(a) Height

Age (years)	Black males (cm)			White males (cm)			Black females (cm)			White female (cm)		
	C3	C50	C97	C3	C50	C97	C3	C50	C97	C3	C50	C97
2	75.7	82.5	89.0	80.5	87.3	95.7	74.9	81.7	88.5	79.9	86.0	94.4
3	83.9	91.2	98.2	86.8	93.9	102.6	83.3	90.6	97.8	86.6	93.2	102.5
4	91.6	99.4	106.9	93.3	100.6	109.7	91.2	99.0	106.8	93.2	100.5	110.6
5	98.5	106.7	114.7	99.4	107.2	116.7	97.8	106.3	114.7	99.6	107.6	118.4
6	104.5	113.4	122.0	105.1	113.3	123.4	104.1	113.2	122.3	105.6	114.2	125.8
7	109.6	119.2	128.6	110.3	119.1	129.9	109.1	118.8	128.4	111.1	120.3	132.6
8	113.6	123.9	134.2	115.7	125.2	136.8	112.8	122.9	133.0	116.4	126.2	139.2
9	118.3	129.2	140.2	121.9	132.1	144.8	118.2	129.1	139.9	121.9	132.2	145.8
10	123.7	134.9	146.6	128.0	138.9	152.6	124.3	136.2	148.0	127.4	138.3	152.5
11	128.4	140.1	152.5	133.3	145.0	159.8	129.7	142.5	155.1	133.1	144.5	159.1
12	131.9	144.6	158.1	138.6	151.1	167.0	135.5	148.4	161.2	139.0	150.7	165.7
13	135.7	149.9	164.7	144.5	157.7	174.8	141.1	153.4	165.5	144.4	156.4	171.5
14	141.1	156.6	172.1	151.0	164.8	182.7	144.9	156.5	168.0	148.4	160.6	175.7
15	147.3	162.9	177.8	156.9	171.1	189.4	146.6	158.0	169.2	150.9	163.0	177.8
16	152.8	167.3	180.8	160.9	175.1	193.4	147.3	158.7	169.9	152.1	164.2	178.6
17	156.3	169.9	182.2	162.9	176.9	194.9	147.7	159.1	170.5	152.8	164.7	178.8
18	158.0	171.1	183.0	163.7	177.5	195.1	147.9	159.5	170.9	153.2	165.0	178.8
19	158.0	171.1	182.9	164.2	177.7	194.9	147.4	159.0	170.5	153.3	165.0	178.5
20	156.7	169.9	181.9	165.0	178.3	195.0	146.5	158.1	169.6	153.3	164.8	178.0

(b) Weight

Age (years)	Black males (kg)			White males (kg)			Black females (kg)			White females (kg)		
	C3	C50	C97	C3	C50	C97	C3	C50	C97	C3	C50	C97
2	8.7	11.1	14.8	10.3	12.7	16.6	8.7	11.1	14.8	10.3	12.7	16.6
3	10.3	13.0	17.0	11.4	14.2	19.0	10.3	13.0	17.0	11.4	14.2	19.0
4	12.2	15.3	19.8	12.7	16.0	21.7	12.2	15.3	19.8	12.7	16.0	21.7
5	14.2	17.7	22.8	14.2	18.0	24.8	14.2	17.7	22.8	14.2	18.0	24.8
6	16.0	20.0	25.8	15.8	20.3	28.5	16.0	20.0	25.8	15.8	20.3	28.5
7	17.7	22.0	28.8	17.6	22.8	32.7	17.7	22.0	28.8	17.6	22.8	32.7
8	19.1	24.0	32.1	19.6	25.8	37.6	19.1	24.0	32.1	19.6	25.8	37.6
9	20.9	26.4	36.8	22.0	29.0	43.0	20.9	26.4	36.8	22.0	29.0	43.0
10	23.1	29.6	43.3	24.4	32.5	48.8	23.1	29.6	43.3	24.4	32.5	48.8

11	25.0	32.6	50.0	27.1	36.3	55.0	25.0	32.6	50.0	27.1	36.3	55.0
12	26.8	35.6	56.2	30.3	40.7	62.0	26.8	35.6	56.2	30.3	40.7	62.0
13	29.2	39.6	62.5	34.2	46.1	70.3	29.2	39.6	62.5	34.2	46.1	70.3
14	32.1	44.7	69.1	38.9	52.4	79.8	32.1	44.7	69.1	38.9	52.4	79.8
15	35.7	49.9	74.5	43.7	58.7	88.9	35.7	49.9	74.5	43.7	58.7	88.9
16	39.5	54.2	78.2	47.7	63.9	96.0	39.5	54.2	78.2	47.7	63.9	96.0
17	43.0	56.9	80.4	50.5	67.4	100.6	43.0	56.9	80.4	50.5	67.4	100.6
18	45.3	58.1	81.6	52.2	69.5	103.2	45.3	58.1	81.6	52.2	69.5	103.2
19	47.1	58.9	84.0	53.4	71.0	104.9	47.1	58.9	84.0	53.4	71.0	104.9
20	48.8	59.8	87.8	54.5	72.4	106.5	48.8	59.8	87.8	54.5	72.4	106.5

(c) BMI

Age (years)	**Black males (kg/m^2)**			**White males (kg/m^2)**			**Black females (kg/m^2)**			**White female (kg/m^2)**		
	C3	**C50**	**C97**	**C3**	**C50**	**C97**	**C3**	**C50**	**C97**	**C3**	**C50**	**C97**
2	12.8	16.7	21.0	14.7	16.9	20.8	13.5	16.7	21.2	12.6	15.5	19.7
3	12.3	15.4	19.1	13.5	15.7	19.8	12.7	15.3	18.8	12.5	15.4	19.8
4	13.3	15.7	18.4	13.0	15.2	19.5	13.2	15.5	18.6	12.5	15.4	19.8
5	13.6	15.6	18.5	12.8	15.1	19.7	13.3	15.4	18.5	12.4	15.5	20.1
6	13.5	15.5	18.6	12.8	15.2	20.0	13.3	15.4	18.8	12.4	15.6	20.6
7	13.6	15.6	18.5	13.0	15.4	20.6	13.3	15.5	19.3	12.5	15.8	20.9
8	13.7	15.7	18.9	13.2	15.8	21.4	13.2	15.6	20.2	12.8	16.0	21.2
9	13.8	15.9	20.5	13.6	16.3	22.2	13.1	15.8	21.7	13.1	16.4	21.6
10	13.9	16.2	23.0	13.9	16.7	22.9	13.2	16.4	24.0	13.5	16.9	22.2
11	13.9	16.5	24.5	14.2	17.1	23.7	13.4	17.1	26.2	13.9	17.4	23.2
12	14.2	16.9	25.5	14.6	17.6	24.7	13.8	18.0	28.1	14.4	18.1	24.4
13	14.6	17.5	26.7	15.1	18.3	25.8	14.5	19.1	29.7	14.9	18.8	25.7
14	15.0	18.1	27.8	15.7	19.1	27.0	15.3	20.1	31.0	15.4	19.5	27.0
15	15.3	18.7	27.3	16.3	19.8	28.3	16.0	21.0	32.1	15.8	20.2	28.4
16	15.7	19.2	26.6	16.9	20.5	29.5	16.5	21.7	32.8	16.2	20.8	29.6
17	16.1	19.6	26.6	17.4	21.2	30.5	16.9	22.2	33.2	16.5	21.3	30.8
18	16.5	19.9	27.1	17.9	21.7	31.5	17.2	22.5	33.6	16.7	21.8	31.8
19	16.9	20.2	27.9	18.3	22.3	32.4	17.5	22.8	34.1	16.9	22.1	32.8
20	17.3	20.5	29.0	18.7	22.8	33.3	17.8	23.2	34.6	17.1	22.5	33.8

(d) Waist circumference

Age (years)	Black males (cm)			White males (cm)			Black females (cm)			White females (cm)		
	C10	**C50**	**C90**	**C10**	**C50**	**C90**	**C10**	**C50**	**C90**	**C10**	**C50**	**C90**
9	51.1	55.4	63.8	51.0	57.1	65.7	48.7	54.5	66.6	50.3	57.2	70.0
10	52.0	56.8	66.4	52.9	59.1	69.0	49.9	56.1	69.0	50.7	57.8	71.1
11	53.0	58.3	69.4	54.8	61.1	72.4	51.6	58.3	72.1	51.9	59.4	73.3
12	54.1	59.9	72.5	56.8	63.3	75.8	53.7	60.9	75.9	53.8	62.0	76.8
13	55.6	61.9	75.6	58.8	65.7	79.3	55.8	63.6	79.9	56.0	64.8	80.5
14	57.5	64.1	78.4	60.9	68.1	83.2	57.8	66.2	83.7	57.4	66.7	83.2
15	59.4	66.3	80.2	63.0	70.4	87.3	59.2	68.2	86.7	58.1	67.9	85.2
16	60.9	67.9	81.2	65.0	72.8	90.8	60.1	69.6	89.1	59.5	70.0	88.1
17	62.2	69.2	81.7	66.7	75.1	92.7	60.7	70.8	91.2	61.3	72.5	91.6
18	63.7	70.9	83.0	67.9	77.4	92.9	63.1	73.9	95.9	61.6	73.2	92.9
19	64.2	71.5	83.4	68.2	79.7	92.9	61.5	72.5	94.7	59.5	71.3	90.8
20	64.2	71.8	83.6	66.4	82.0	93.4	57.8	68.7	90.3	56.6	68.3	87.4

(e) Hip circumference

Age (years)	Black males (cm)			White males (cm)			Black females (cm)			White females (cm)		
	C2.3	**C50**	**C97.7**	**C2.3**	**C50**	**C97.7**	**C2.3**	**C50**	**C97.7**	**C2.3**	**C50**	**C97.7**
9	51.3	57.2	67.4	56.3	63.3	76.1	49.7	57.7	70.4	55.7	63.9	80.1
10	59.5	66.4	78.3	61.5	69.1	82.6	60.1	69.7	85.0	61.0	70.3	85.2
11	65.1	72.9	86.4	66.5	74.5	88.6	65.9	76.6	94.0	65.2	75.7	89.6
12	67.4	75.9	91.0	69.9	78.2	92.6	69.4	80.7	99.2	69.5	80.8	94.4
13	69.2	78.3	95.0	73.0	81.5	96.0	74.5	86.3	105.4	74.1	86.0	99.6
14	71.8	81.2	98.2	76.6	85.4	100.2	79.5	91.6	110.9	78.1	90.0	103.7
15	75.2	84.5	100.4	80.2	89.2	104.2	82.0	94.0	113.0	80.9	92.6	106.0
16	78.7	87.6	102.0	82.5	91.6	106.5	83.5	95.2	113.4	82.7	94.0	107.3
17	80.3	88.9	102.3	83.5	92.5	107.2	85.1	96.7	114.7	83.7	94.7	107.8
18	81.3	89.9	103.0	84.0	92.9	107.3	86.6	98.7	117.7	84.3	95.1	107.9
19	80.1	88.6	101.5	85.2	94.1	108.2	84.5	97.0	117.5	84.8	95.3	108.0
20	78.2	86.6	99.3	86.9	95.8	109.8	81.1	94.0	116.4	85.2	95.5	108.1

Chapter 4 Characterisation of Adolescent Growth

Adolescent growth and BMI and their associations with early childhood growth in an urban South African cohort

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Note: Due to document formatting (possibly the multiple section breaks), MS word has inserted a "4" between the chapter number and table or figure number in the legends. For example, Table 4-1 is labeled as Table 4-4-1. Correcting these manually removes the cross referencing, so they have not been corrected.

Erratum: On page 96 of this thesis, this statement appears; "The variances explained by the SITAR model were: male height 98.9%, female height 98.6%, male weight 94.1%, female weight 92.4%, male BMI 90.5% and female BMI 92.1%". The numbers in table 1 on page 97 are not consistent with these. This was an error during the publication of the manuscript. The figures given in the text are correct.

4.1 Abstract

Background

The timing and magnitude of adolescent growth may be influenced by ethnicity and early life factors. We aimed to (i) characterise ethnic differences in the magnitude, timing and intensity of adolescent growth in height, weight and BMI; (ii) assess the effect of early childhood growth on adolescent growth in black children.

Methods

Data were from the Birth to Twenty Plus cohort (Bt20+) in Johannesburg, South Africa (n=3273). Height, weight and BMI were modelled with ethnic comparisons using the SuperImposition by Translation and Rotation (SITAR) for 2089 participants who had data from 7-23 years. Relative weight gain and relative linear growth between 0-24 months and 24-60 months were generated. Multiple regression analyses were used to assess associations between childhood and adolescent growth.

Results

White children were 5 cm (SE: 0.7) taller than black children through adolescence. Black boys had a later timing of adolescent height (0.65 years ± 0.12) than white boys, which in black girls was 0.24 years (0.11) earlier than in white girls. Black girls had faster BMI velocity than white

girls. Among black children, birth weight and both relative weight gain 0-24 and relative linear growth between 3-24 months and 24-60 months were positively associated with the magnitude of adolescent growth and negatively associated with timing.

Conclusion

Sex dimorphism in ethnic differences in timing of adolescent height growth may reflect some yet unexplained drivers for rapid weight gain and obesity in black females but not black males. Rapid weight gain in early life may contribute to faster adiposity accrual in adolescence.

Key words: puberty, South Africa, children, obesity, growth

4.2 Background

Puberty is a period of rapid growth with significant changes in height, weight and body composition. Globally, there is a secular trend towards earlier puberty driven by improving socio-economic conditions (Ali, Lestrel, & Ohtsuki, 2000; Jones et al., 2009), both of which are more apparent in transitioning than developed societies (249). In South Africa, a secular change towards earlier puberty as assessed by age at menarche has been observed in black females (190) and by skeletal age particularly in black children (250). However, black males experience a six-month delay in skeletal maturity compared to white males, which is not seen in females (Cole et al., 2015). The adolescent growth spurt is a prominent feature of pubertal development and also provides an objective measure of pubertal timing. However, there is a paucity of data describing the adolescent growth spurt of South African children.

Transitioning societies like South Africa are experiencing a double burden of malnutrition (underweight and obesity) and the adolescent growth spurt may contribute to the rise in the prevalence of obesity. Data from the Bt20+ cohort have shown that the incidence of overweight and obesity was highest between the ages of 11 and 18 years in females (62), leading to a higher prevalence in black female than male adolescents (251). Changes in adolescent body composition may reflect metabolic changes during puberty (252), and both the timing of puberty (52,253) and BMI gain (194) are associated with early life growth. Rapid weight gain in early childhood is associated with advanced skeletal maturity (138), earlier age at menarche and advanced Tanner stages (254), while faster linear growth in infancy is associated with an earlier age at peak height velocity (APHV) during puberty (255).

The adolescent growth spurt has been studied largely in relation to height and weight and there are far fewer studies reporting on BMI (adiposity marker) during puberty (256,257). Thus, the aims of this study were two-fold (i) to characterise differences between black and white children in the magnitude (size), timing (tempo) and intensity (velocity) of adolescent growth (height, weight and BMI); and (ii) to assess the effect of early life growth on the magnitude, timing and intensity of adolescent growth in black participants. We hypothesized that there would be ethnic differences in size (large or small relative to the sample mean curve), tempo (early or delayed growth relative to the sample's mean curve) and velocity (steeper or flatter relative to the sample's mean curve) of adolescent growth in height, weight and BMI. Further, faster growth in early childhood would be associated with an earlier tempo of adolescent growth in height, weight and BMI.

4.3 Methods

4.3.1 Participants and settings

Data for this study were obtained from the Birth to Twenty Plus (Bt20+) birth cohort, a longitudinal study of 3273 singleton children born in the Greater Johannesburg region in South Africa between 23 April and 8 June 1990 (Richter, Yach, Cameron, Griesel, & de Wet, 1995; Richter, Norris, & De Wet, 2004; Yach et al., 1991). Due to the demographics of the population in Johannesburg at the time of enrolment, only a small number of white children were enrolled in the original cohort. This and the greater loss to follow up of these children in early childhood

made it impossible to calculate conditional variables for white children. Thus, we did not include white children in determining the association between early growth events and adolescent growth and development. However, an additional number of white children born during the same period in 1990 were recruited at age 9 years (n=157) which made it possible to model adolescent growth. For the current study, growth was modelled for 2089 (895 black males; 115 white males; 970 black females & 109 white females) participants who had data between 7 and 23 years. There was an average of 7.0 (± SD 3.3) observations during this period per child and the total number of observations per group was 6440 for black males; 674 for white males; 6387 for black females & 670 for white females. All participants and their guardians provided written informed assent and consent, respectively. Ethics approval was obtained from the University of the Witwatersrand Committee for Research on Human Subjects (M010556).

4.3.2 Anthropometric measurements

Anthropometric measurements were collected annually using standard methods (Cameron, 1984). Weight at birth was collected from birth records while from 3 months to 23 years it was measured by field workers. Weight was measured to the nearest 0.1kg using an electronic scale (Dismed, Miami, FL, USA). Birth lengths were not routinely measured at delivery and these data was not available. Recumbent length was measured from 3 months to 2 years of age by trained field workers. From 2 to 23 years, standing height was measured without shoes to the nearest 0.1cm using a Harpenden stadiometer (Holtain, Crymych, UK). BMI was computed from length/height and weight using a standard formula.

4.3.3 Socio-demographic variables

In early childhood, mothers or caregivers of the participants completed interviewer-administered structured questionnaires when participants were 6 months, 1 year and 2 years of age. Data on maternal education, parity, age and information on physical assets were collected. An index of socio-economic status (SES) of the household was calculated by summing the main tangible assets owned in the household, such as a television, car, washing machine, refrigerator and telephone (258).

4.3.4 Growth modelling

Height, weight and BMI from age 7 to 23 years were modelled using the SuperImposition by Translation and Rotation (SITAR; Version 1.0.10 in R version 3.4.2,), a shape invariant model with a single fitted curve that summarises individual growth patterns with three parameters (259). The subject-specific random effects (α_i, β_i, γ_i) correspond to the size (magnitude), tempo (timing) and velocity (intensity) of height, weight or BMI, and make individual curves as similar in shape as possible. The random effects allow for variation along the x and y axes in the units of the measurement, throughout the period of measurement i.e. 7 to 23 years for the current study. Magnitude refers to a shift on the y-axis which indicates how large or small an individual is relative to the sample mean curve while timing refers to a shift on the x-axis, which indicates how early or delayed an individual is relative to the sample mean curve. Intensity represents the shrinking or stretching of the age-scale affecting the steepness of the curve, giving an indication of how fast or slow an individual is relative to the sample mean curve. Data were cleaned using

the plotclean and velout functions in SITAR, which identify outliers with abnormal velocities. Models were fitted at various degrees of freedom, chosen in decreasing order from the first whole number below the mean number of observations. The Bayesian Information Criterion (BIC) was used to assess model fit where a lower BIC indicates a better model fit. The best model was rerun after excluding observations with residuals greater than 2 units, which improved model fit. Models for weight and BMI were fitted on a log(y). The results from log transformed data were interpreted as sympercents (260). Given that we are interested in ethnic differences, i.e. differences between black and white participants, models were fitted for males and females separately but black and whites combined. The ethnicity variable was added to the final model to allow for ethnic comparisons, using white participants as reference.

4.3.5 Statistical analysis

Multiple regression analyses were performed using Stata version 13.1 (StataCorp, USA). Using the random effects obtained from the SITAR models, multiple linear regression analyses were performed to assess the effect of early life growth (birth to 5 years) on adolescent growth. Weight-for-age Z-scores (WAZ) were generated using the World Health Organization (WHO) 2006 child growth standards for children between birth and 5 years (67). To address collinearity between the independent variables and to separate out the effects of linear growth and weight gain, standard residuals were obtained (261). Relative weight gain between birth and 24 months was obtained by regressing weight at 24 months on current length (24 months) and previous length (12 months) and weight (12 months and birth). Relative weight gain between 24 and 60 months was obtained by regressing weight at 60 months on current length (60 months) and

previous length and weight (24, 36 and 48 months). In a similar manner, relative linear growth between 3 months and 24 months and between 24 and 60 months were obtained by regressing on previous length but not weight (261). All models were adjusted for maternal education, parity, age and SES.

4.4 Results

The number of participants and observations for each SITAR model are presented in ***Table 4-4-1***. The variances explained by the SITAR model were: male height 98.9%, female height 98.6%, male weight 94.1%, female weight 92.4%, male BMI 90.5% and female BMI 92.1%. Unadjusted and SITAR adjusted individual curves and the sample's mean curves are presented in ***Figure 4-4-1*** to demonstrate model fit. Mean distance and velocity curves for height, weight and BMI, stratified by sex and race, are presented in ***Figure 4-4-2***.

4.4.1 Ethnic differences in height, weight and BMI

There were ethnic differences in height, weight and BMI (***Table 4-4-2***) which are presented as mean differences (SE). Where data were log transformed, data are presented as sympercentages (SE). There were ethnic differences in the magnitude (size), timing (tempo) and intensity (velocity) parameters for height in both males and females. White males and females were 5.5 cm (0.7) and 5.1 cm (0.30) taller than black males and females respectively ($p < 0.001$). Peak height velocity was delayed by 0.65 years (0.12) in black compared to white males ($p < 0.001$) while it was earlier by 0.23 years (0.11) in black than white females ($p = 0.03$). Ethnic

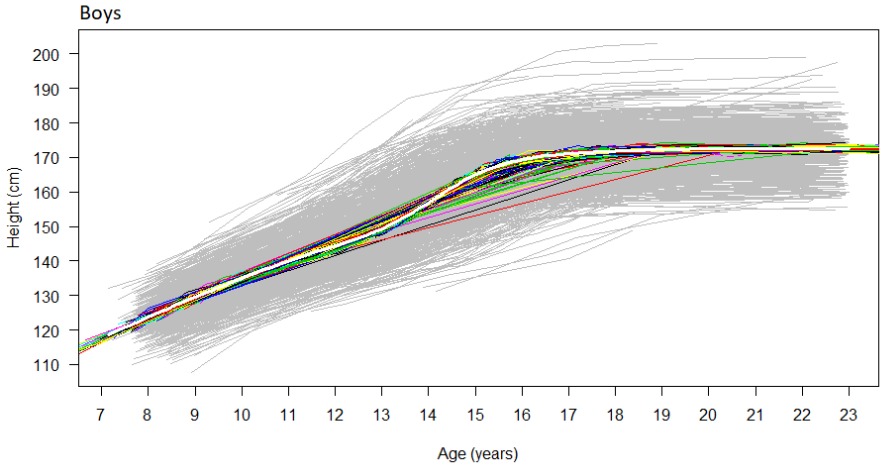
differences in weight were observed among males but not females. Black males were 15% (0.02) lighter than white males. Black males also had lower BMI (-8% ± 0.002) and slower BMI intensity (-27% ± 0.06) than white males. Black females had 16% (SE: 0.06) faster BMI intensity than white females (p = 0.01).

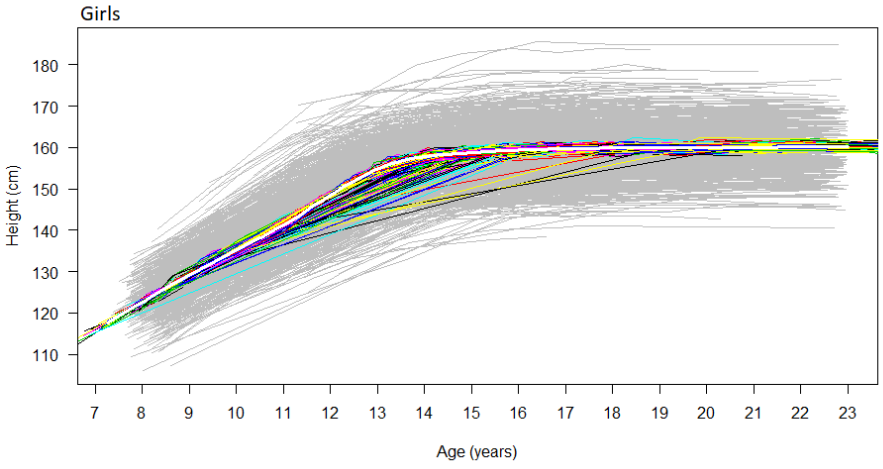
Table 4-4-1: Sample size and outcomes of SITAR model fitting for height, weight and BMI

	Males			**Females**		
	Height (cm)	Weight (kg)	BMI (kg/m^2)	Height (cm)	Weight (kg)	BMI (kg/m^2)
No. subjects/observations	1018/7122	1018/7122	1015/7122	1079/7454	1089/7454	1089/7454
Degrees of freedom	6	5	3	6	4	4
Residual SD$^{\delta}$	0.86	0.04	0.63	0.75	0.04	0.04
Size-tempo correlation	0.19	0.08	0.20	0.31	0.32	-0.13
Size-velocity correlation	0.18	0.22	0.68	0.04	0.24	0.63
Tempo-velocity correlation	-0.67	-0.64	-0.06	-0.61	-0.14	-0.34
Variance explained (%)	99	96	94	99	96	95

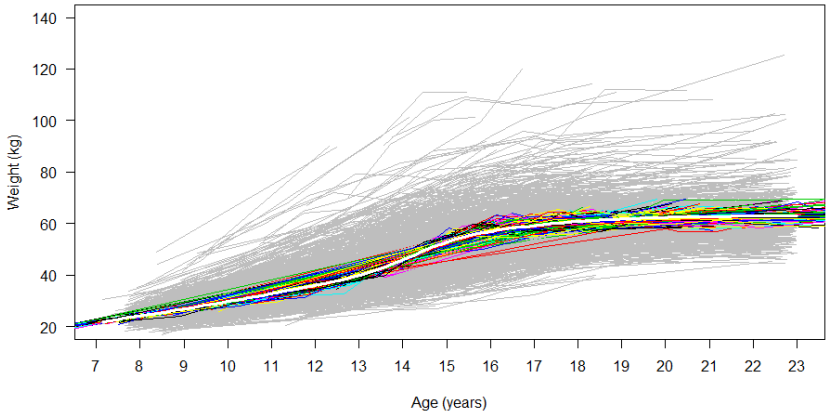
$^{\delta}$ For height, the residual SD is in cm while for weight and BMI it is based on log transformed data

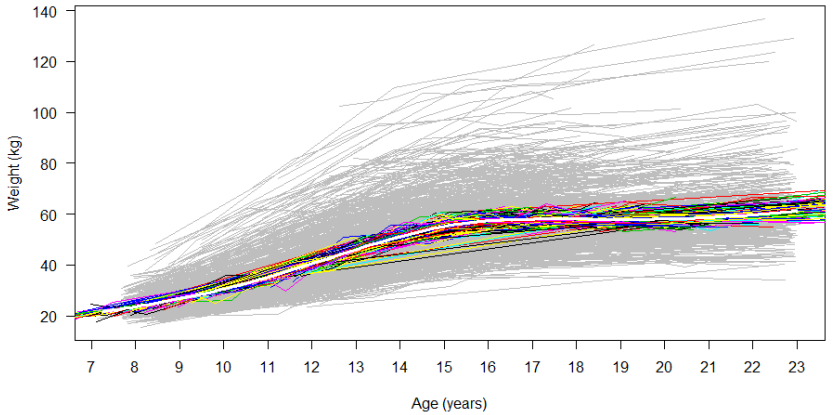
(a) Height





(b) Weight





(c) BMI

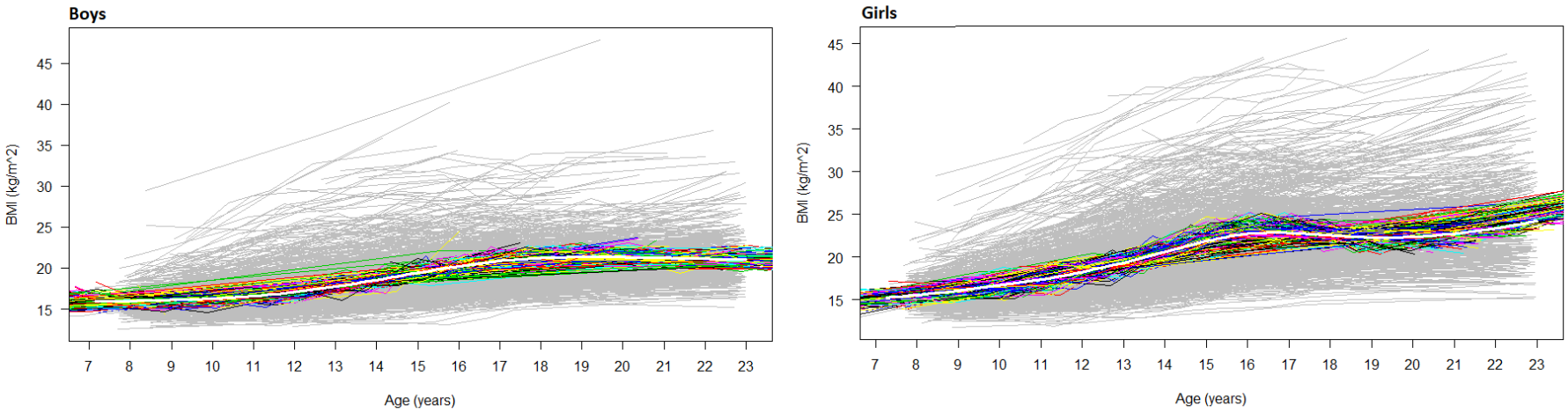


Figure 4-4-1: Unadjusted (grey) and SITAR adjusted (colours) individual plots and mean plot (white) to demonstrate the fitting of the SITAR model for raw data

Table 4-4-2: Ethnic differences (black and white using white as reference group) in SITAR parameters for height, weight and BMI; mean difference (standard error). Magnitude & intensity are in the units of the outcome variable (e.g. cm & cm/yr for height) and timing is in years

	Males			Females		
	Height (cm)	Weight (kg)$^{\delta}$	BMI (kg/m^2)$^{\delta}$	Height (cm)	Weight (kg)$^{\delta}$	BMI (kg/m^2)$^{\delta}$
Size parameter	-5.49 (0.71)***	-0.15 (0.02)[a]***	-0.08 (0.02) [b]***	-5.10 (0.66)***	-0.02 (0.02)	0.03 (0.02)
Tempo parameter	0.65 (0.12)***	0.26 (0.15)	-0.06 (0.30)	-0.23 (0.11)*	0.11 (0.14)	-0.15 (0.24)
Velocity parameter	-0.18 (0.02)***	-0.16 (0.02)[a]***	-0.27 (0.06) [b]***	-0.05 (0.02)**	0.01 (0.03)	0.17 (0.06)[c]**

[δ] Output based on log transformed data as specified below. For interpretation, mean difference is multiplied by 100 and interpreted as percentage difference

[a] Model based on log(weight): black males were 15% lighter and 16% slower weight gain than white males

[b] Model based on log(BMI): black males had 8% lower BMI and 27% slower BMI gain than white males

[c] Model based on log(BMI): black females had 18% faster BMI gain than white females

*p < 0.05; **p < 0.01; ***p < 0.001

4.4.2 Associations between early life growth and SITAR random effects timing, magnitude and intensity

The associations between early life factors and adolescent growth parameters are presented in ***Table 4-4-3***; results are presented as β ± SE. For adolescent height, rapid linear growth between 3-24 months (-0.17 years ± 0.06 & -0.14 years ± 0.04) and 24-60 months (-0.13 years ± 0.05 & -0.10 years ± 0.04) were associated with an earlier timing of adolescent height in males and females, respectively. Both birth weight z-score (~1.2 cm ± 0.2), and rapid linear growth between 3-24 months (~3.2 cm ± 0.2) and 24-60 months (~2.5 cm ± 0.2) were positively associated with the magnitude of adolescent height while rapid weight gain 24-60 months (~0.4 cm ± 0.2) was negatively associated with the magnitude of adolescent height in both sexes (Table 3a)

For adolescent weight, (Table 3b), relative weight gain between 0-24 months (~ -0.3 years ± -0.06) and relative linear growth between 0-24 months (~ -0.2 years ± 0.06) in both sexes, as well as relative linear growth between 24-60 months (~ 0.2 years ± 0.05) in females, were associated with an earlier adolescent timing of adolescent weight. Birth weight z-score (~ +3 - 4% ± 0.005), relative weight gain between 0-24 months (~ +3 - 5% ± 0.005) and 24-60 months (~ +3 - 4% ± 0.005), and relative linear growth between 3-24 months (~ +5% ± 0.006) and 24-60 months (~ +3% ± 0.0065) were all positively associated with the magnitude of adolescent weight in both sexes.

For adolescent BMI (Table 3c), relative weight gain between 0-24 months (~ -0.4 years ± 0.1) and 24-60 months (~ -0.2 years ± 0.1) in both sexes, and relative linear growth between 3-24 months (-0.20 years ± 0.08) in females, were associated with an earlier timing of adolescent BMI. Birth weight z-score (~ +2 - 3% ± 0.006), relative weight gain between 0-24 months (~ +3 - 5% ± 0.006) and 24-60 months (~ +4% ± 0.006) were positively associated with the magnitude of adolescent BMI in both sexes.

Between 2.1 and 10.8% of the variance in intensity and between 5.5 to 15.2% of the variance in timing in both sexes for height, weight and BMI could be explained by early childhood growth and confounders (maternal education, parity, age and SES). The variance explained for magnitude of height, weight and BMI was greater, ranging from 19.2 to 52.3% for both sexes. ***Table 4-4-4*** shows a summary of the regression analyses which highlight the associations between early childhood growth and earlier timing of adolescent height, weight and BMI and positive associations with the magnitude of adolescent body size.

Table 4-4-3: The effect of early life growth and environment on the timing, magnitude and intensity of pubertal height, weight, and BMI change in black children; beta coefficient (standard error). All models were adjusted for maternal education, parity, age and SES.

(a) Height

Independent Variables	Males			Females		
	Timing (years)	**Magnitude (cm)**	**Intensity (cm/yr)**	**Timing (years)**	**Magnitude (cm)**	**Intensity (cm/yr)**
Birth weight z-score	-0.060	1.260***	0.008	0.063	1.334***	-0.000
	(0.051)	(0.206)	(0.006)	(0.037)	(0.186)	(0.006)
Relative weight gain 0-24m	-0.083	0.393	-0.005	-0.166***	0.093	0.022**
	(0.053)	(0.216)	(0.007)	(0.042)	(0.215)	(0.007)
Relative weight gain 24-60m	-0.025	-0.457*	-0.010	-0.092*	-0.521**	0.007
	(0.052)	(0.211)	(0.006)	(0.038)	(0.191)	(0.006)
Relative linear growth 3-24m	-0.175**	3.287***	0.019**	-0.140***	3.219***	0.029***
	(0.056)	(0.225)	(0.007)	(0.041)	(0.208)	(0.007)
Relative linear growth 24-60m	-0.132**	2.668***	0.019**	-0.099*	2.542***	0.017*
	(0.050)	(0.203)	(0.006)	(0.039)	(0.198)	(0.007)
R-squared	**0.055**	**0.520**	**0.054**	**0.119**	**0.523**	**0.108**

(b) Weight

Independent Variables	Males			Females		
	Timing (years)	**Magnitude (kg)**	**Intensity (kg/yr)**	**Timing (years)**	**Magnitude (kg)**	**Intensity (kg/yr)**
Birth weight z-score	-0.072	0.041***	0.012	0.006	0.033***	-0.003
	(0.056)	(0.005)	(0.008)	(0.049)	(0.006)	(0.007)
Relative weight gain 0-24m	-0.274***	0.033***	0.012	-0.303***	0.054***	0.028***
	(0.059)	(0.006)	(0.008)	(0.056)	(0.007)	(0.008)
Relative weight gain 24-60m	-0.088	0.037***	0.013	-0.105*	0.033***	0.005
	(0.057)	(0.006)	(0.008)	(0.050)	(0.007)	(0.007)
Relative linear growth 3-24m	-0.190**	0.047***	0.006	-0.203***	0.053***	0.015*
	(0.061)	(0.006)	(0.009)	(0.054)	(0.007)	(0.007)
Relative linear growth 24-60m	-0.079	0.033***	0.003	-0.175***	0.027***	0.010
	(0.055)	(0.005)	(0.008)	(0.052)	(0.007)	(0.007)
R-squared	**0.088**	**0.359**	**0.021**	**0.152**	**0.294**	**0.049**

(c) BMI

Independent Variables	Males			Females		
	Timing (years)	Magnitude (kg/m^2)	Intensity ($kg/m^2/yr$)	Timing (years)	Magnitude (kg/m^2)	Intensity ($kg/m^2/yr$)
Birth weight z-score	-0.102	0.027***	0.042*	-0.002	0.018**	-0.003
	(0.101)	(0.006)	(0.021)	(0.071)	(0.006)	(0.016)
Relative weight gain 0-24m	-0.390***	0.034***	0.048*	-0.447***	0.053***	0.028
	(0.107)	(0.006)	(0.022)	(0.083)	(0.007)	(0.018)
Relative weight gain 24-60m	-0.233*	0.042***	0.059**	-0.179*	0.040***	0.023
	(0.103)	(0.006)	(0.021)	(0.074)	(0.006)	(0.016)
Relative linear growth 3-24m	-0.071	0.009	0.012	-0.202*	0.012	0.012
	(0.111)	(0.007)	(0.023)	(0.080)	(0.007)	(0.018)
Relative linear growth 24-60m	-0.003	-0.001	0.002	-0.118	-0.005	-0.015
	(0.099)	(0.006)	(0.020)	(0.076)	(0.006)	(0.017)
R-squared	**0.059**	**0.193**	**0.047**	**0.100**	**0.209**	**0.030**

*** p<0.001, ** p<0.01, * p<0.05

4.5 Discussion

We set out to assess ethnic differences in the size achieved, the timing and the rate of adolescent growth in height, weight and BMI, and to test the association between early childhood growth and adolescent growth. We were able to show ethnic differences in all SITAR parameters (i.e. magnitude, timing and intensity) for height, weight and BMI during puberty. There were differences in height (all parameters) in both sexes, weight and BMI (magnitude and intensity) in males, while in females there were only differences in BMI intensity. Historically, South African black children have been shown to be shorter, lighter and have less fat than white children (183,185,235). Data from the current study suggest that there has been a positive secular change in weight and BMI in black females but height lags behind. Previous findings in the same cohort have shown that the prevalence of overweight and obesity in black females is nearly double that in white females in late adolescence (27.9 vs 17.1% at age 17 years) (251). The fact that black females had slower growth velocity in height but similar weight velocity may have contributed to the greater BMI velocity in black than white females and thus to an increased risk of obesity in late adolescence and adulthood. Adult black females have the highest prevalence of overweight and obesity in the country (107).

We found that APHV was 8 months later in black than white males, while it was 3 months earlier in black than white females. A similar pattern has been described in Sudanese adolescents, with a delay of 1 year in APHV being observed in Sudanese males compared to their British peers living in the UK, but not in females (262). Additionally, the delay in APHV in our cohort is corroborated by the finding in the same cohort of a 6-month delay in skeletal

maturity in black males compared to their white peers but not in females during puberty. It was suggested that this delay may be due to male susceptibility to stress (189). However, the timing of puberty is associated with obesity (263) and it is possible that the sexual dimorphism in ethnic differences in APHV may be related to the rising obesity prevalence in black females.

South African urban black females have experienced a secular trend towards earlier puberty with the age at menarche now being similar in black and white females (190). At the same time, the similarity in weight between black and white females suggests that black females are experiencing a positive secular change in weight which is not evident in black males. Thus, factors driving the upsurge in obesity in adolescence in black females may also influence the earlier height tempo in black females (264).

Puberty is also influenced by environmental factors and its timing is associated with early childhood growth. We found significant associations between early childhood growth and the magnitude, timing and intensity of adolescent growth in height, weight and BMI in black children. Generally, rapid weight gain and linear growth in childhood are associated with larger body size, earlier timing (consequently earlier age at peak velocity) and greater intensity of adolescent growth. In both boys and girls, early childhood height and BMI were associated with earlier and faster pubic hair development in the Bt20+ cohort (193). Previous data also from the Bt20+ cohort showed that rapid weight gain in early childhood was associated with the risk of being in the early-onset obese to morbid obese trajectory (194). In our study in females, linear growth between 3-24 months was positively associated with adolescent BMI values and negatively associated with BMI tempo (earlier onset of BMI gain).

The period in early childhood (infancy vs. toddler) in which growth failure or rapid growth occurs, is significant for later life outcomes. Growth failure between birth and 12 months is a better predictor of short stature than growth failure in the toddler period (34). In our study, rapid weight gain between 0-24 months was positively associated with pubertal height, weight and BMI while rapid weight gain between 24-60 months was negatively associated with pubertal height but positively associated with weight and BMI, leading to shorter but fatter individuals. Antonisamy and colleagues found that weight gain in early infancy (0-3 months) was positively associated with adult height, while weight gain in childhood through adolescence (6.5 – 15 years) was negatively associated with adult height (265). Similarly, He and Karlberg found negative associations between BMI gain between 2 to 8 years and adolescent height gain. They attributed to the potential adverse effects of adolescent adiposity on GH and IGF-I secretion in that period (266).

Rapid weight gain, which may result from catch up growth in the first few months of postnatal life, is common in early childhood (Cameron, Pettifor, De Wet, & Norris, 2003; Cole, Singhal, Fewtrell, & Wells, 2016), possibly related to poor birth outcomes (268). A combination of low birth weight and rapid postnatal growth is associated with greater risk of later obesity. On the contrary, poor birth outcomes with no catch-up growth may contribute to early childhood undernutrition which is linked to poor health outcomes in later life. Stunting at 2 years is negatively associated with schooling outcomes (133). This presents an intervention conundrum as both rapid weight gain and linear growth are associated with increased risk of obesity and poor health outcomes in later life (261,268). Data from five LMIC cohorts including Bt20+

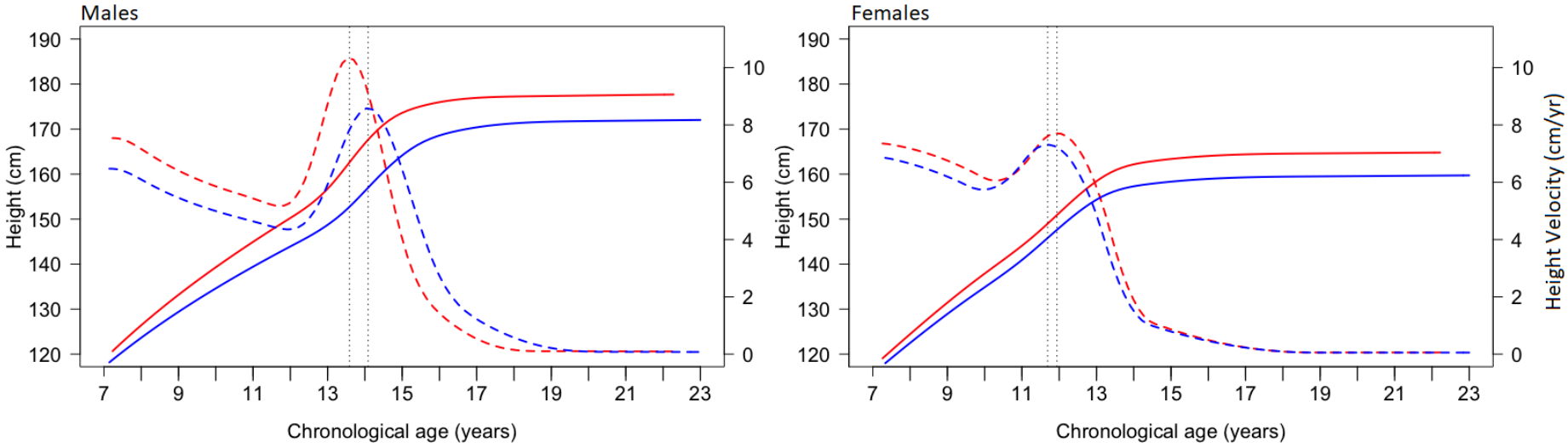
showed that lower birth weight and rapid weight gain irrespective of whether the children were small-for-gestational age or not, were associated with poor health outcomes (133).

This study provides insight into the biology of adolescent growth in a sample of black and white, male and female children in an urban community in South Africa, an upper middle-income country. Additionally, it provides insight into the relationship between early life and adolescent growth. Adolescent growth was assessed using SITAR which has previously been used to model adolescent growth in height, weight and BMI (Blackwell et al., 2017; Cao, Hui, & Wong, 2018; Cole, 2018; Frysz, Howe, Tobias, & Paternoster, 2018; Martin & Valeggia, 2018; Simpkin, Sayers, Gilthorpe, Heron, & Tilling, 2017). This study however has limitations. Associations between early life and adolescent growth could only be assessed for black children due to small number of white children in the early childhood years in this study. Thus, the associations between early life and adolescent growth may not be generalizable to other groups.

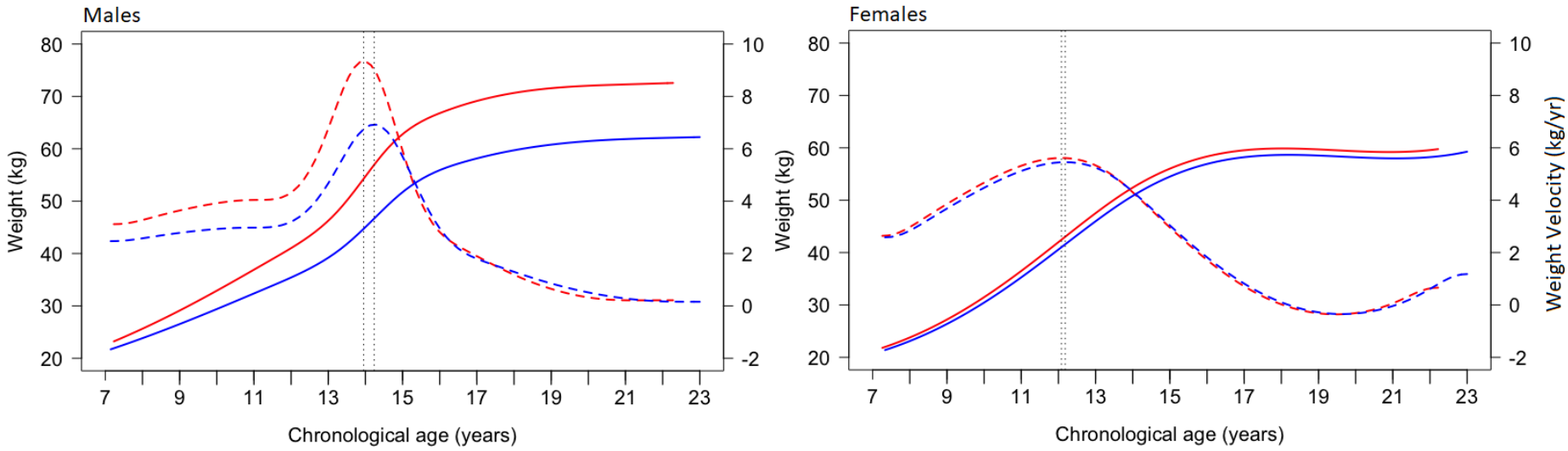
4.6 Conclusion

In conclusion, we found ethnic differences in the magnitude, timing and intensity of adolescent growth in height, weight and BMI. White children were taller and had greater height velocity than black children. APHV occurred later in black than white males while earlier in black than white females. Black females also had a faster BMI velocity than white females. Rapid growth in early childhood is associated with an earlier onset and greater magnitude of adolescent growth. Monitoring and managing weight gain in early childhood could assist in curbing the rise in adolescent obesity.

(a) Height



(b) Weight


Males
Weight (kg)
Chronological age (years)
Females
Weight (kg)
Weight Velocity (kg/yr)
Chronological age (years)

(c) BMI

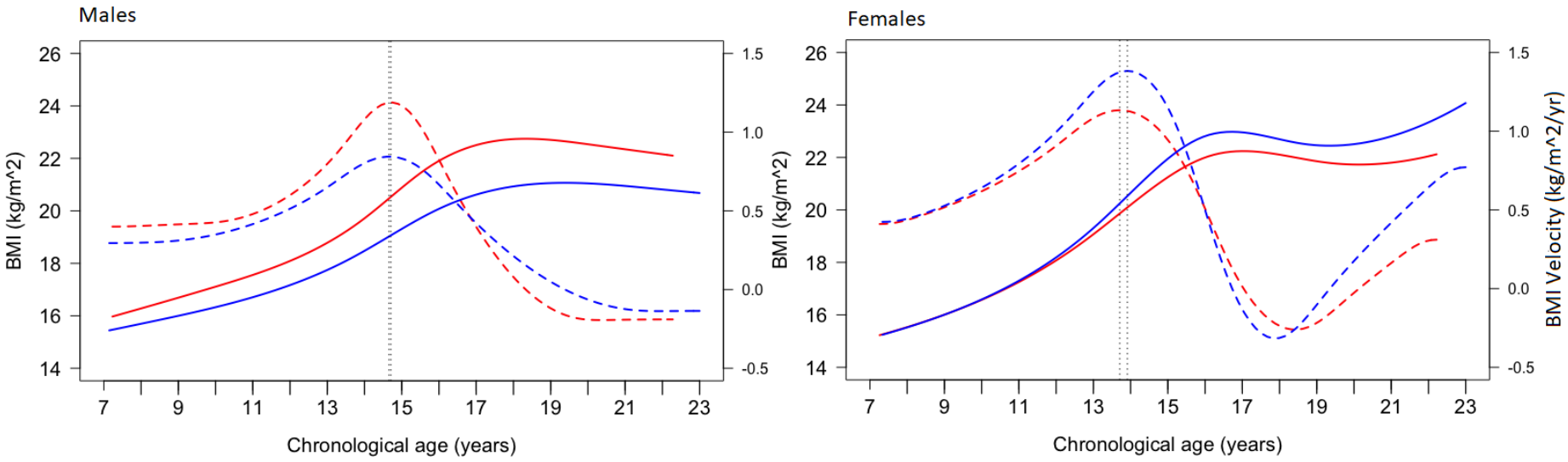


Figure 4-4-2: Ethnic differences (Black = blue and White = red; N = 895 BM, 115 WM, 970 BF, 109 WF) in distance and velocity growth curves for (a) height, (b) weight, and (c) BMI.

The vertical lines represent age at peak velocity (APV). APV and peak velocities (PV) are presented for black vs. white males and females respectively: height – males (APV = 14.1 vs. 13.6 years & PV = 8.7 vs. 10.6 cm/yr) and females (APV = 11.7 vs. 12.0 years; PV = 7.3 vs. 7.7 cm/yr); weight – males (APV = 14.2 vs. 14.0 years & PV = 6.7 vs. 9.0 kg/yr) and females (APV = 12.9 vs. 12.9 years; PV = 5.5 vs. 5.8 kg/yr); BMI – males (APV = 14.8 vs. 14.5 years & PV = 1.3 vs. 2.1 kg/m2/yr) and females (APV = 13.4 vs. 13.0 years; PV = 1.3 vs. 1.0 kg/m2/yr)

Table 4-4-4: Summary of associations between early childhood and pubertal growth for (a) males and (b) females. Upward arrows indicate significant positive associations, downward arrow indicate significant negative associations while horizontal lines indicate insignificant associations.

(a)

Early childhood	Puberty	Size	Tempo	Velocity
Birth weight Z-score	Weight	↑	—	—
	Height	↑	—	—
	BMI	↑	↓	↑
Weight gain 0-24m	Weight	↑	↓	—
	Height	↑	—	—
	BMI	↑	↓	↑
Weight gain 24-60m	Weight	↑	↓	↑
	Height	↓	—	—
	BMI	↑	↓	↑
Linear growth 0-24m	Weight	↑	↓	—
	Height	↑	↓	↑
	BMI	—	—	—
Linear growth 24-60m	Weight	↑	—	—
	Height	↑	↓	↑
	BMI	—	—	—

(b)

Early childhood	Puberty	Size	Tempo	Velocity
Birth weight Z-score	Weight	↑	—	—
	Height	↑	—	—
	BMI	↑	—	—
Weight gain 0-24m	Weight	↑	⇣	↑
	Height	—	⇣	↑
	BMI	↑	⇣	—
Weight gain 24-60m	Weight	↑	—	—
	Height	⇣	⇣	—
	BMI	↑	⇣	—
Linear growth 0-24m	Weight	↑	⇣	—
	Height	↑	⇣	↑
	BMI	↑	⇣	—
Linear growth 24-60m	Weight	↑	⇣	—
	Height	↑	⇣	↑
	BMI	—	—	—

Chapter 5 Adolescent Growth & Adult Outcomes

The association between the timing, intensity and magnitude of adolescent growth and body composition

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Note: Due to document formatting (possibly the multiple section breaks), MS word has inserted a "0" between the chapter number and table or figure number in the legends. For example, Table 5-1 is labeled as Table 5-0-1. Correcting these manually removes the cross referencing, so they have not been corrected.

5.1 Abstract

Objectives

Adult body composition is associated with the timing of puberty but there are few longitudinal studies in low- and middle-income countries to assess these trends. Thus, the aims of this study were to assess (i) the role of pubertal development on adolescent growth, and (ii) the association between adolescent change in height, weight and BMI and early adult height, weight, body fat and lean mass.

Subjects and Methods

Data from the prospective longitudinal Birth to Twenty Plus (Bt20+) cohort were used. Adolescent growth spurts for height, weight and BMI were modelled using the SuperImposition by Translation and Rotation (SITAR) growth curve model from 7 to 23 years. Tanner maturity scores were summarised as pubertal trajectories from 9 to 16 years of age. Early adult height, weight, BMI and DXA derived body composition were obtained between the ages of 21-24 years from 1881 black South African participants. Linear regression analyses were used to assess associations.

Results

Adolescents with an earlier onset of puberty were heavier in childhood and had an earlier timing and greater intensity (velocity) of weight gain in adolescence. The intensity of adolescent weight gain was positively associated with adult BMI and fat mass index (FMI) in females. Early timing of adolescent BMI gain was associated with increased weight and BMI in adult females and FMI in adult males. Females who had a later timing of adolescent height gain were shorter in adulthood. Achieving peak weight velocity prior around age of peak height velocity was associated with lower BMI and fat mass in both sexes.

Conclusion

This study confirms the apparent adverse consequences of excessive weight gain prior to puberty on early adulthood BMI. Factors that contribute to an asynchronous timing of ages of peak weight and peak height velocities may accentuate the risk of adult obesity.

Key words:

obesity, puberty, fat mass, lean mass, childhood, SITAR

5.2 Background

The prevalence of obesity is escalating globally, but more rapidly in low- and middle-income countries (LMIC) (64), which is contributing to an epidemiological transition of disease burden from communicable to non-communicable diseases (272). Obesity is associated with an increased risk of morbidity and mortality, partially through an increased risk of cardiometabolic diseases in adulthood. Increased waist circumference, body mass index (BMI) and whole body fat mass are associated with markers of chronic inflammation (273), while increased truncal fat mass is associated with dyslipidaemia and insulin resistance (274). When viewed through the lifecourse, the prevalence of obesity rises in adolescence (61) and early adulthood (275), influenced by the adolescent growth spurt and a resurgence in BMI velocity in early adulthood (276). Thus, a lifecourse approach is needed to assess the influence of growth and body composition accrual during these two critical periods on the aetiology of obesity.

Adolescence is characterised by physiological and life style changes, which contribute to the accumulation and central distribution of adipose tissue, increasing the risk of obesity in this period (61). However, there may be population differences in the pattern and the timing of the development of obesity in the lifecourse. During the childhood and adolescence period, the incidence of obesity in the United Kingdom (UK) is highest in late childhood (7 - 11 years) (277), whereas in South Africa it is highest in adolescence (11 – 18 years) (62). Additionally, the patterns of the sex differences which emerge during adolescence may differ between LMIC and high-income countries (HIC). Data from the United States of America (USA) show that there are no sex differences in the prevalence of obesity during adolescence (278), while there is a higher

male prevalence in Sweden (279). However, our data from South Africa show that in females the prevalence rises with age while in males it remains constant through adolescence to age 17 years, when females have double the prevalence of overweight and obesity than males (251).

The impact of these different patterns on relationship between adolescent growth and early adult body composition is unclear. There is a paucity of studies investigating the relationship between pubertal development and adolescent growth and their relationships to adult outcomes in LMIC. Data from our group have shown that early puberty (54) and early BMI gain (194) are associated with higher BMI and risk of obesity in young adulthood. However, these studies did not assess the components of BMI (fat and lean mass). Additionally, it is suggested that the rates of adipose tissue accrual generally slow after peak height velocity (61), and few studies have used age of peak height velocity (APHV) as a marker in pubertal development to assess the period in adolescence at which adipose tissue accrual or weight gain may influence adult outcomes (275). Therefore, the aims of this longitudinal study of South African urban black children through adolescence and into young adulthood, were to assess the associations between the magnitude (size), timing (tempo) and intensity (velocity) of adolescent height, weight and BMI gain and adult fat mass, lean mass, height and weight.

5.3 Methods

5.3.1 Study design and setting

Data for this study were from Birth to Twenty Plus (Bt20+) cohort, which followed 3273 black and white children born in the City of Johannesburg Municipal area between April and June 1990 . Details of the cohort are elsewhere but are briefly summarised here (216–218). Mothers who had permanent residence or continued residence for longer than 6 month and had singleton pregnancies were included (216). Data were collected at yearly data collection cycles from birth to 19 years. In young adulthood, data were collected between 21 and 24 years (21+ years) and 1881 black participants who had data in young adulthood were included in the current study. All participants above the age of 18 years provided written informed consent while at younger ages, their guardians provided written informed consent and the participants provided assent (from 11 years). Ethics approval was obtained from the University of the Witwatersrand Committee for Research on Human Subjects (M010556)

5.3.2 Anthropometric measurements

Height and weight were measured from 7 to 21+ years using the method of Lohman et al (225). Stretch height was measured using a Harpenden Stadiometer (Holtain, U.K.) to the nearest 0.1 cm without shoes. Weight was measured on an electronic scale to the nearest 0.1kg. BMI was derived from height and weight. The International Obesity Task Force (IOTF) age and sex specific cut-offs for BMI were used to evaluate nutritional status (overweight/obese vs.

normal/underweight) between the ages of 7 and 18 years (280). The adult BMI cut-offs were used to determine nutritional status beyond 18 years.

5.3.3 Body composition outcome variables

Whole body (excluding head because of hair weaves) composition was assessed by dual x-ray absorptiometry (DXA) using standard techniques. All scans were conducted by a qualified technician on a Hologic QDR 4500A machine when participants were 21+ years old to estimate bone mineral content (BMC), fat-free mass (FFM), fat mass (FM), abdominal visceral adipose tissue (VAT), and abdominal subcutaneous adipose tissue (SAT). Fat-free soft tissue mass (FFSTM) was calculated as the difference between FFM and BMC, while the fat mass index (FMI) and fat-free mass index (FFMI) were calculated by dividing FM (kg) and FFSTM (kg) respectively by the square of height (m^2). These scans were analysed using Hologic APEX 3.1 software (281). A spine phantom was used for daily calibration, and coefficients of variation during the course of the study were less than 1% for total FM and FFSTM. DXA-determined VAT and SAT were computed as described previously (281). SAT was estimated by summing the subcutaneous fat measured from the DXA image on each side of the abdominal cavity, and subcutaneous fat overlying the abdominal cavity which was determined by modelling (281). DXA-VAT was estimated by subtracting SAT from the total abdominal fat determined by DXA (281).

5.3.4 Pubertal trajectories

The determination of pubertal development was based on self-reported assessments using line drawings of the Tanner sexual maturation stages (282) for pubic hair and breast/genital development as aids. Self-assessment has been validated in this setting (283). Pubertal trajectory classes were computed from the Tanner sexual maturation scale data between ages 9 to 16 years using latent class growth analyses (LCGA) by Lundeen et al (193). LCGA were conducted on girls and boys separately resulting in three classes for pubic hair development in each sex. For each sex, class 1 encompassed the group of children who had the lowest Tanner stage at 9 years of age and whose pubertal progression was slowest over time, class 3 included those with the earliest pubertal onset and fastest progression through puberty, and class 2 was defined as an intermediate group (193).

5.3.5 SITAR modelling of adolescent growth

The SuperImposition by Translation and Rotation (SITAR; Version 1.0.10 in R version 3.4.2,) was used to model height, weight and BMI between 7 and 23 years. SITAR fits a single curve and adjusts individual curves to a similar shape, using the subject-specific random effects of magnitude (size), timing (tempo) and intensity (velocity) (230). The random effects (α_i, β_i, γ_i) allow for horizontal and vertical shifts along the x and y axes in the units of the measurement, to measure the timing of growth and the size of the individual relative to the mean curve. Age at peak height velocity was derived from the tempo (timing) random effect. Intensity gives an indication of slope of the curve to demonstrate how fast or slow the change is in an individual

relative to the velocity of the mean curve. The best fitting model was chosen based on the lowest Bayesian Information Criterion (BIC). The pubic hair classes were used to stratify participants according to the timing of development in SITAR models.

5.3.6 Statistical Analysis

Data were analysed using Stata version 13.1 (Stata-Corp LP, College Station, Texas, USA). The data is presented as means (SD) for continuous variables and frequencies (proportions) for categorical data. Sex differences in continuous variables were assessed using the two-sample t-test while the Pearson chi-squared test was used to assess differences in categorical variables. To assess the association between the timing of weight or BMI gain and adult outcomes, the age at peak height velocity (APHV) was subtracted from the age at peak weight (APWV) or BMI (APBV) velocity. Using this difference, participants were grouped into tertiles for early, average and late peak weight or BMI velocity. One-way analyses of variance (ANOVA) with Bonferroni multiple comparisons test were used to assess differences in adult outcomes between the three groups. Multiple linear regression analyses were performed to assess adolescent factors associated with adult height, weight, BMI, FM, FFSTM, FMI, FFMI, VAT & SAT. Separate models for adolescent height, weight and BMI as exposures were performed. To adjust for pubertal development, the pubic hair development latent classes were included in the models. The variance inflation factor was used to assess multicollinearity. The Q-ladder function which performs a QQ-plot of residuals was used to assess appropriate transformation for dependent variables and all outcome variables were log transformed.

5.4 Results

5.4.1 Sex differences in body composition and size in adults

As adults (age 21-24 years old), males were taller and had greater FFSTM than females ($p < 0.001$). Females were slightly heavier ($p < 0.05$) and had greater BMI, FM, VAT and SAT ($p < 0.001$) (***Table 5-0-1***).

Table 5-0-1: Sex differences in adult body size and body composition

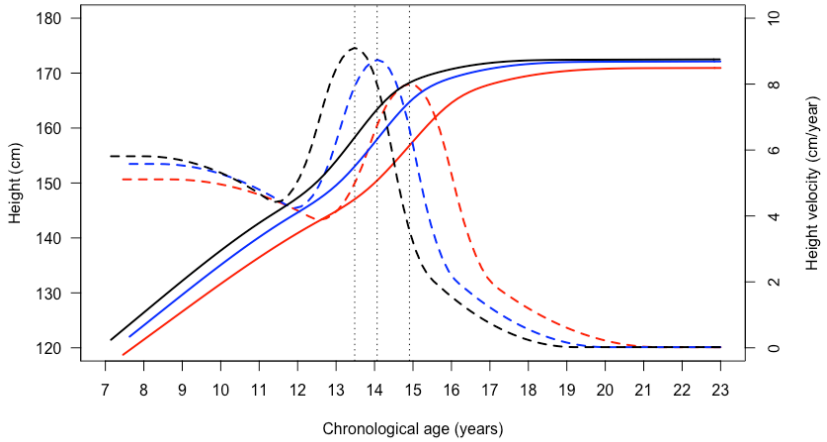
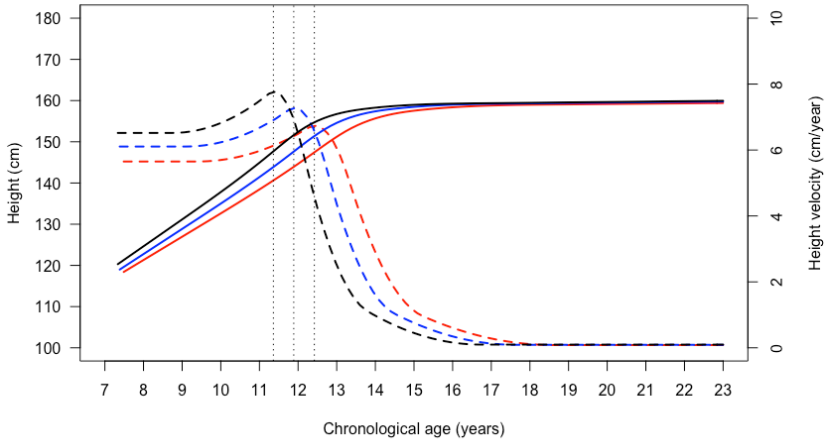
Variables	Males	Females	P-value[ϕ]
N	903	978	
Height (cm)	171.7 (6.6)[a]	159.7 (6.1)	< 0.001
Weight (kg)	63.5 (11.3)	65.3 (16.2)	0.015
BMI (kg/m^2)	21.5 (3.6)	25.6 (6.1)	< 0.001
Fat mass (kg)	12.8 (6.1)	25.0 (9.9)	< 0.001
Fat-free soft-tissue mass (kg)	44.1 (5.9)	33.7 (5.2)	< 0.001
Fat mass-to-fat-free mass ratio	0.3 (0.1)	0.7 (0.2)	< 0.001
Visceral adipose tissue (g)	222.0 (91.6)	288.9 (175.8)	< 0.001
Subcutaneous adipose tissue (g)	451.7 (367.4)	1489.2 (718.8)	< 0.001
Pubic hair development classes[b]			
Class 1 (slow developers)	188	178	
Class 2 (average developers)	394	405	
Class 3 (fast developers)	93	100	

[a]mean ± SD; [ϕ]Differences were assessed using a t-test

[b]Pubertal class 3 had the earliest onset and faster progression of pubic hair development while class 1 had the most delayed and slowest progression. Class 2 was intermediate.

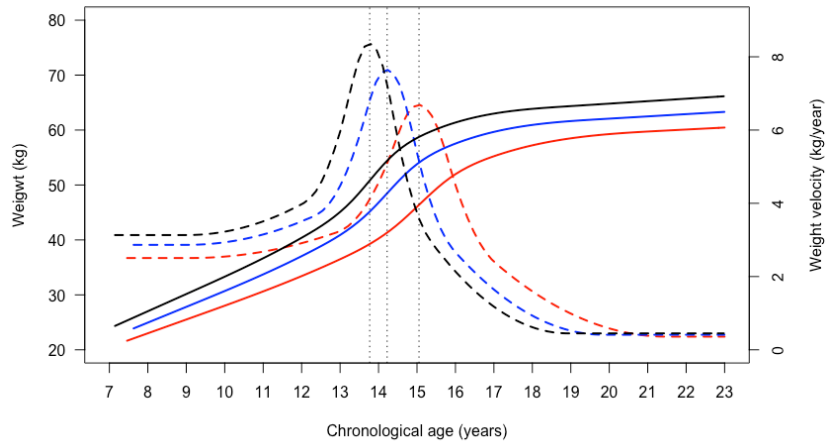
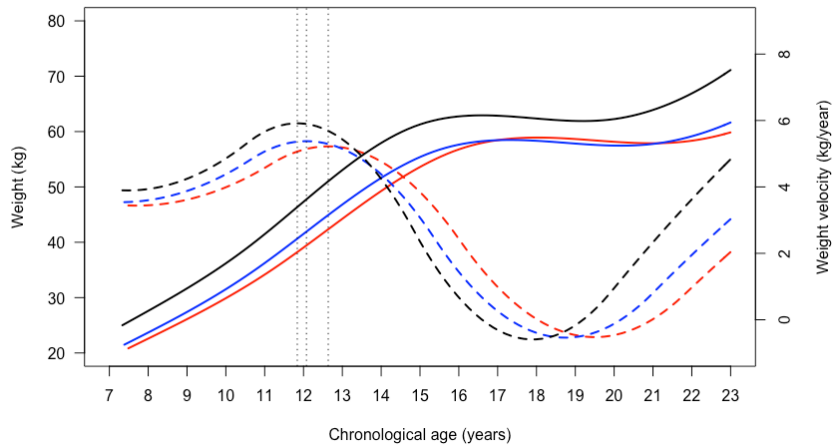
5.4.2 Effect of puberty (pubic hair development) on adolescent growth in height and weight and adult size (Figure 5-0-1 & Table 5-0-2)

During adolescence, males with the earliest or intermediate onset of pubic hair development (classes 2 and 3) were taller ($p < 0.05$) and heavier ($p < 0.001$) than those with a slowest onset (pubic hair class 1), but the differences in height disappeared in adulthood. In females, the timing of the onset of pubic hair development was not associated with early adult height. Both males and females with the earliest onset of pubic hair development (class 3) were heavier and had faster weight gain than those with later onset ($p < 0.001$). Females in the earliest onset group experienced a resurgence in weight gain in early adulthood. Early and average developers had an earlier timing of the growth spurts for height and weight in both sexes.

A – Height Males	B – Height Females
	

(a) Height males: APV & PV; class 1 (14.9 years & 8.9 cm/year), class 2 (14.1 years & 8.7 cm/year), class 3 (13.5 years & 9.1 cm/year)

(b) Height females: APV & PV; class 1 (12.4 years & 6.7 cm/year), class 2 (11.9 years & 7.3 cm/year), class 3 (11.4 years & 7.7 cm/year)

C – Weight Males	D – Weight Females
	

(c) Weight males: APV & PV; class 1 (15.1 years & 6.7 kg/year), class 2 (14.2 years & 7.7 kg/year), class 3 (13.8 years & 8.4 kg/year)

(d) Weight females: APV & PV; class 1 (12.6 years & 5.2 kg/year), class 2 (12.1 years & 5.4 kg/year), class 3 (11.8 years & 5.9 kg/year)

Figure 5-0-1: The effect of latent classes of pubertal development on the adolescent growth in height (a & b) and weight (c & d). Pubic hair was stratified to 3 classes, class 1 (red), class 2(blue) and class 3 (black).

Table 5-0-2: Differences in the magnitude, timing and intensity of adolescent changes in height, weight and BMI between groups of pubertal development latent classes; class 1 (late), class 2 (average) and class 3 (early). The later development group (class 1) is the reference.

Variable	SITAR Parameter	Males		Females	
		Early	Average	Early	Average
N: participants/observations		921/6647		859/6380	
Height (cm)	Magnitude	1.50 (0.74)*	1.13 (0.52)*	0.29 (0.64)	0.24 (0.48)
	Timing	-1.42 (0.11)***	-0.8 (0.08)***	-1.23 (0.11)***	-0.63 (0.08)***
	Intensity	0.13 (0.02)***	0.09 (0.02)***	0.14 (0.02)***	0.08 (0.01)***
Weight (kg)	Magnitude	4.37 (1.02)***	2.07 (0.71)**	4.00 (1.22)***	-0.46 (0.91)
	Timing	-1.29 (0.16)***	-0.84 (0.11)***	-0.92 (0.17)***	-0.60 (0.13)***
	Intensity	0.22 (0.04)***	0.13 (0.03)***	0.12 (0.03)***	0.03 (0.02)
BMI (kg/m^2)	Magnitude	1.19 (0.26)***	0.30 (0.18)	1.67 (0.42)***	-0.15 (0.31)
	Timing	-0.57 (0.29)*	-0.57 (0.20)**	-1.00 (0.19)***	-0.47 (0.15)**
	Intensity	0.29 (0.08)***	0.12 (0.06)*	0.12 (0.06)*	-0.004 (0.04)

*p < 0.05, **p < 0.01, ***p < 0.001

5.4.3 Adolescent height growth and adult body composition and size (Table 5-0-3a)

The magnitude of adolescent height gain was positively associated with adult height, weight, FM, and FFSTM in both sexes, as well as FMI, VAT and SAT in males. In both sexes, the later onset (timing) of adolescent height gain was associated with a reduction in all measures of adult body composition and weight, but not height in males. However, in females an earlier timing of adolescent height gain was associated with taller adult height. Faster height gain was associated

with taller adult height and VAT/SAT ratio, but lower weight and all measures of body composition in males. The intensity of height gain in females had no influence on final body composition or size. In the regression models, pubertal development classes had limited effects on adult size or body composition. Those with the earliest onset of pubic hair development (class 3) had greater adult weight, BMI, fat mass and FMI than later developers. (***Table 5-0-2***). Although alone pubic hair development had no effect on height in females, when assessed with the magnitude, timing and intensity of adolescent height gain, the earliest onset of pubic hair development was associated with shorter adult height.

The variance explained by the model (magnitude, timing and intensity of adolescent height and pubic hair development classes) was approximately 96% for adult height in both sexes, for adult weight 23.5% in males & 13.6% in females and for FFSTM mass 32.4% in males and 26.3% in females. Adolescent height gain explained less than 10% of the variance in the other adult variables.

5.4.4 Adolescent weight gain and adult body composition and size (Table 5-0-3b)

The magnitude of adolescent weight gain was positively associated with adult height and all measures of adult body composition in both sexes. In males, the timing of adolescent weight gain was negatively associated with adult height and fat mass but positively associated BMI and the fat-free soft tissue mass index. In males and females, the intensity of adolescent weight gain was negatively associated with adult height, but positively with a number of variables associated with body composition, such as BMI and fat free soft tissue mass. The variance in adult height

explained by the model (magnitude, timing and intensity of adolescent weight and pubic hair development classes) was ~23% and 9% in males and females respectively. Between ~29% and ~72% and between ~35% and ~ 66% of the variance in adult body composition (excluding VAT/SAT ratio) could be explained by the parameters of adolescent weight gain and pubic hair development classes, in males and females respectively.

5.4.5 Adolescent BMI gain and adult body composition and size (Table 5-0-3c)

The magnitude of adolescent BMI gain has the greatest associations with adult body composition variables in both males and females. The other measures of adolescent BMI gain (timing and intensity) had few significant associations with adult height or body composition, except for adult weight and BMI in females. An earlier timing of adolescent BMI gain in males was associated with a significant increase in FMI but a reduction in FFMI. Between ~32% and ~75% and between ~37% and ~ 74% of the variance in adult body composition (excluding VAT/SAT ratio) could be explained by the parameters of adolescent BMI gain and pubic hair development classes, in males and females respectively.

5.4.6 Effects of the timing of peak weight velocity and peak BMI velocity in relation to age of peak height velocity on adult outcomes (Table 5-0-4)

An earlier peak of weight velocity was associated with taller adult height but lower weight, BMI and FFMI (***Table 5-0-4a***). In males, an early peak weight velocity was associated with lower fat-free soft tissue mass while in females it was associated with lower fat mass. In females, early

peak weight velocity was associated with both lower FMI, FFMI, VAT and SAT. The effect of timing of peak BMI velocity in relation to peak height velocity on adult anthropometry was diametrically opposite in the two sexes. Early onset peak BMI velocity resulted in decreased adult FM, FFSTM, FMI, FFMI, VAT and SAT in males, but the converse in females (Table 3b). In males, weight, BMI, FM and FMI were lowest for those who had their BMI peak around APHV. (***Table 5-0-4b***).

5.5 Discussion

We investigated the association between pubertal development and adolescent growth and their association with young adult height and body composition. While adolescent body composition may reflect concurrent metabolic changes in puberty (252), both the timing and magnitude of adolescent BMI gain are associated with adult morbidity. Dietz suggested that the association between adolescent obesity and morbidity may be driven by an increase in total body fat and redistribution of fat mass to central depots during puberty (284). We measured whole body and abdominal (VAT & SAT) fat mass, whole body fat-free mass, weight and BMI in early adulthood and found that the magnitude of weight and BMI gain achieved in adolescence was better at predicting adult body composition than intensity and timing. These results support He and Karlberg's findings that BMI status, i.e. BMI achieved at a particular age, was more important for subsequent body size than the rate of BMI gain (285). However, the intensity of adolescent weight and BMI gain were also positively associated with adult weight, BMI, fat mass, FMI, and SAT but not VAT, although not to the same degree as the magnitude of weight and BMI gain. The association of the timing of adolescent height gain, where early height gain

was associated with greater whole body fat and fat-free mass and both abdominal SAT and VAT, is supported by previous findings (253).

Adolescence is a critical period for obesity, which may predispose to increased risk of excess adiposity in this period and beyond. Thus, assessing changes in adolescent BMI may give insight into drivers of excess fat. BMI is easy to measure, making it a useful but crude proxy for adiposity. It has been reported that FMI and FFMI have no additional value in predicting the metabolic syndrome over BMI in children and adolescents (286). However, the strength of overweight status to predict excess FMI is influenced by sex and ethnicity. Weber et al found that the positive predictive value of overweight status in measuring excess FMI was considerably lower in black (35.9% & 30.3%) than white (65.4% & 52.2%) and Mexican American (73.3% & 68.3%) adolescent males and females, respectively (287). There are also ethnic differences in fat distribution with African American children having lower visceral fat but similar subcutaneous and whole body fat than white American children (288). We were unable to confirm this, due to the low number of white participants in the 21 to 24-year age group, who were thus not included in the current study. Notwithstanding, the nutrition transition could be more prominent in the black population in South Africa, with black females having an increasingly higher prevalence of overweight and obesity (251) and BMI velocity (276) in adolescence than South African white females.

The current study adds to our knowledge of the contribution of adolescence to the risk of both excess fat mass (whole body and abdominal) and BMI gain in adulthood. There is a growing

interest in the age group 18 to 25 years (289) as these early adult years may represent another critical period for the rise in obesity. Our previous findings on this cohort show that black females experience a resurgence in BMI gain in early adulthood period (18+ years), which is faster than that in white females (276). In the current study, a similar resurgence in weight velocity in females was observed among those with early onset of pubic hair development when the data were stratified by pubertal development. These women were heavier in childhood through adolescence and had the earliest onset of puberty and age of peak weight velocity. Thus, a cascade of events starting with increased childhood adiposity to the earliest onset of puberty, and greater and earlier weight gain in adolescence leads to a resurgence of weight gain in the early adulthood period. Differences in BMI between those who become overweight before or after the age of 25 years emerge in mid-childhood (140) underscoring the persistence of early onset obesity through adolescence to adulthood.

The importance of childhood weight gain in females is emphasised in the sex differences in the association of the timing of peak BMI gain relative to APHV with adult outcomes. The age of peak BMI velocity (APBV) is an important landmark in the development of adolescent adiposity as Guo and colleagues found that BMI size at maximum velocity was the most important predictor of adult total body fat and percent body fat (290). It has also been hypothesised that the rate of adiposity gain decreases after APHV (61). Thus, assessing these patterns in relation to biological maturity aligns individuals on a common landmark to adjust for variations in developmental trajectories in order to estimate true phenotypic differences and their potential impact. Sex differences in adolescent height, weight and BMI were more strongly associated with biological maturity than with chronological age (291). When combined in a model with

maturational status, chronological age was not significantly associated with weight status while early maturity was associated with greater weight status (292), emphasising the importance of maturational status in assessing these patterns. In this study, we found that APBV earlier than APHV was associated with greater early adult BMI, whole-body fat mass, FMI and subcutaneous adipose tissue in females but the reverse was true in males. Guo et al found that BMI patterns during and post adolescence were more important for adult total body fat and percent body fat status than earlier patterns for both sexes while for women, childhood patterns were also important (290). Thus, an asynchrony of weight, body composition and height gain in adolescence may predispose to increased risk of adult obesity.

The timing of peak velocity for weight (APWV) and components of body composition (fat mass and fat-free mass) are said to occur around APHV (293), although others have observed delays in attainment of APWV relative to APHV (294). Previously in this cohort, we found delays of between 0.9 and 1.7 years in the timing of APWV & APBV compared to APHV (276). Findings from the current study show that a synchronised APHV and APWV contributed to the lowest BMI and fat mass in both sexes. In males, we also found that reaching APBV around APHV was associated with the lowest early adult weight, BMI, FM and FMI. This supports findings by Barbour-Tuck et al, who showed that overweight status at APHV was not associated with early adult overweight status in a cohort of adolescent males (275). In females, the earliest APBV group, who had the highest BMI and fat mass, paradoxically had a later APHV. This is surprising given that a greater childhood or early adolescent BMI is associated with an earlier APHV (295). Understanding factors that contribute to an asynchronous timing of the adolescent

growth spurts for height, weight and BMI may improve our understanding of the lifecourse determinants of obesity.

There are a number of strengths of this paper. Firstly, we used multiple indicators of adolescent growth and pubertal development to assess their associations and how they relate to adult outcomes. The SITAR parameters of size (magnitude), tempo (timing) and velocity (intensity) which provide a multidimensional assessment of adolescent growth add to the strengths of this study. In addition, we used pubic hair development to provide an independent measure of the timing of pubertal development. Another strength of this paper is that the data are from a middle-income country where there is a rapid rise in obesity. We also used several indicators of body composition outcome including BMI and DXA derived body composition, which are scarce in these settings. However, the study does have limitations. The sample was exclusively made up of black urban South Africans and thus the findings may not be generalisable to other populations or rural communities. In addition, we did not adjust our analyses for lifestyle factors such as socio-economic status, diet or physical activity. The low number of participants who developed overweight/obesity at APHV may influence the strength of the findings.

5.6 Conclusion

In conclusion, we found that the timing of the adolescent growth spurt for height was negatively associated with early adult BMI, whole body and abdominal fat mass. The magnitude of adolescent weight and BMI gain was more important in determining early adult body

composition than the rate and timing of gain. However, early BMI gain, before APHV, was an important determinant of increased BMI, and whole body and abdominal fat mass. Factors that contribute to an asynchronous timing of the adolescent growth spurts for height, weight and BMI may contribute to an increased risk of obesity, especially in females. Young adult females also experience resurgence in weight gain in early adulthood which is faster among those who were heavier in childhood and adolescence. The period of transition between the teenage years and early adulthood may be a critical period in which intervention may influence the risk of obesity and disease in later life. Strategies to limit the rate of weight gain during late childhood and adolescence might be beneficial for future metabolic health.

Table 5-0-3. Linear regression analyses to assess the effect of the magnitude, timing and intensity of adolescent growth in (a) height, (b) weight, and (c) BMI on adult outcomes, adjusted for pubic hair development classes. Data presented as coefficients (SE). Significance is indicated by asterisks; *** p<0.001, ** p<0.01, * p<0.05

(a) Adolescent height

Adult Variables	Height (cm)	Weight (kg)	BMI (kg/m^2)	Fat mass (g)	Fat free mass (g)	FMI	FFMI	VAT (g)	SAT (g)	VAT/SAT Ratio
Males										
Magnitude	1.005***	0.013***	0.001	0.019***	0.013***	0.007*	0.001	0.008*	0.017**	-0.009*
	(0.009)	(0.001)	(0.001)	(0.003)	(0.001)	(0.003)	(0.001)	(0.004)	(0.006)	(0.004)
Timing	-0.095	-0.057***	-0.056***	-0.129***	-0.042***	-0.129***	-0.041***	-0.107***	-0.194***	0.089*
	(0.073)	(0.009)	(0.009)	(0.029)	(0.008)	(0.029)	(0.008)	(0.030)	(0.048)	(0.036)
Intensity	2.800***	-0.353***	-0.384***	-0.954***	-0.171*	-0.985***	-0.204**	-0.647**	-1.364***	0.743*
	(0.597)	(0.071)	(0.071)	(0.238)	(0.067)	(0.238)	(0.067)	(0.249)	(0.396)	(0.299)
Pubic hair 2	-0.011	0.016	0.016	0.060	-0.021	0.060	-0.021	0.081	0.051	0.030
	(0.118)	(0.014)	(0.014)	(0.047)	(0.013)	(0.047)	(0.013)	(0.049)	(0.078)	(0.058)
Pubic hair 3	-0.273	0.053**	0.056**	0.130	-0.002	0.134*	0.002	0.052	0.155	-0.104
	(0.172)	(0.020)	(0.020)	(0.067)	(0.019)	(0.067)	(0.019)	(0.070)	(0.112)	(0.084)
R-squared	0.967	0.235	0.094	0.098	0.324	0.072	0.069	0.050	0.058	0.030
Females										
Magnitude	1.009***	0.013***	0.001	0.011**	0.013***	-0.002	0.001	0.008	0.004	0.003
	(0.009)	(0.002)	(0.002)	(0.003)	(0.001)	(0.003)	(0.001)	(0.006)	(0.004)	(0.003)
Timing	-0.222**	-0.082***	-0.079***	-0.137***	-0.037***	-0.135***	-0.035***	-0.212***	-0.179***	-0.033
	(0.085)	(0.015)	(0.015)	(0.031)	(0.010)	(0.031)	(0.010)	(0.053)	(0.040)	(0.030)
Intensity	0.886	-0.141	-0.152	-0.271	-0.080	-0.284	-0.094	-0.418	-0.295	-0.122
	(0.505)	(0.087)	(0.087)	(0.194)	(0.065)	(0.195)	(0.066)	(0.333)	(0.253)	(0.188)
Pubic hair 2	-0.099	-0.023	-0.022	-0.041	0.001	-0.041	0.001	-0.115	-0.062	-0.053
	(0.117)	(0.020)	(0.020)	(0.044)	(0.014)	(0.044)	(0.015)	(0.073)	(0.055)	(0.041)
Pubic hair 3	-0.463**	0.047	0.053	0.041	0.019	0.047	0.025	-0.053	0.035	-0.087
	(0.167)	(0.029)	(0.029)	(0.061)	(0.020)	(0.061)	(0.020)	(0.101)	(0.077)	(0.057)
R-squared	0.958	0.136	0.083	0.071	0.263	0.084	0.041	0.052	0.076	0.008

(b) Adolescent weight

Adult Variables	Height (cm)	Weight (kg)	BMI (kg/m^2)	Fat mass (g)	Fat free mass (g)	FMI	FFMI	VAT (g)	SAT (g)	VAT/SAT Ratio
Males										
Magnitude	26.450***	1.065***	0.757***	2.016***	0.811***	1.701***	0.501***	1.504***	2.701***	-1.200***
	(1.893)	(0.024)	(0.033)	(0.121)	(0.029)	(0.129)	(0.032)	(0.142)	(0.219)	(0.187)
Timing	-1.277***	-0.003	0.012*	-0.039*	0.005	-0.027	0.017***	-0.022	-0.045	0.024
	(0.292)	(0.004)	(0.005)	(0.018)	(0.004)	(0.020)	(0.005)	(0.022)	(0.033)	(0.028)
Intensity	-13.109***	0.038	0.190***	-0.048	0.037	0.096	0.182***	0.079	0.109	-0.023
	(2.273)	(0.029)	(0.039)	(0.142)	(0.034)	(0.152)	(0.038)	(0.169)	(0.258)	(0.221)
Pubic hair 2	0.656	-0.000	-0.008	0.018	-0.014	0.009	-0.023*	0.051	-0.019	0.071
	(0.546)	(0.007)	(0.009)	(0.034)	(0.008)	(0.037)	(0.009)	(0.041)	(0.062)	(0.053)
Pubic hair 3	-0.488	0.023*	0.029*	0.044	-0.005	0.050	-0.000	0.003	0.043	-0.040
	(0.793)	(0.010)	(0.014)	(0.049)	(0.012)	(0.053)	(0.013)	(0.058)	(0.090)	(0.076)
R-squared	0.233	0.797	0.570	0.477	0.715	0.381	0.509	0.286	0.346	0.129
Females										
Magnitude	13.117***	1.080***	0.916***	1.718***	0.717***	1.543***	0.537***	2.205***	1.836***	0.369**
	(1.719)	(0.033)	(0.039)	(0.092)	(0.032)	(0.101)	(0.032)	(0.195)	(0.132)	(0.132)
Timing	-0.532	-0.005	0.002	-0.008	-0.007	0.006	0.006	-0.017	0.010	-0.027
	(0.301)	(0.006)	(0.007)	(0.015)	(0.005)	(0.017)	(0.005)	(0.033)	(0.022)	(0.023)
Intensity	-7.187**	0.118**	0.208***	0.279*	-0.023	0.404**	0.103*	0.294	0.582***	-0.288
	(2.289)	(0.043)	(0.052)	(0.119)	(0.043)	(0.131)	(0.042)	(0.258)	(0.174)	(0.174)
Pubic hair 2	0.414	0.012	0.007	0.010	0.021*	0.002	0.015	-0.046	-0.007	-0.040
	(0.537)	(0.010)	(0.012)	(0.028)	(0.010)	(0.031)	(0.010)	(0.060)	(0.040)	(0.040)
Pubic hair 3	-0.095	0.013	0.014	-0.012	0.003	-0.008	0.008	-0.075	0.011	-0.086
	(0.759)	(0.014)	(0.017)	(0.039)	(0.014)	(0.043)	(0.014)	(0.082)	(0.055)	(0.055)
R-squared	0.093	0.773	0.661	0.602	0.632	0.526	0.554	0.352	0.499	0.023

(c) Adolescent BMI

ADULT VARIABLES	Height (cm)	Weight (kg)	BMI (kg/m^2)	Fat mass (g)	Fat free mass (g)	FMI	FFMI	VAT (g)	SAT (g)	VAT/SAT Ratio
Males										
Magnitude	-0.982	1.021***	1.033***	2.477***	0.598***	2.473***	0.596***	1.861***	3.611***	-1.756***
	(3.164)	(0.052)	(0.037)	(0.176)	(0.062)	(0.170)	(0.044)	(0.204)	(0.304)	(0.267)
Timing	-0.176	-0.001	0.001	-0.018*	0.003	-0.016*	0.005**	-0.013	-0.023	0.010
	(0.142)	(0.002)	(0.002)	(0.008)	(0.003)	(0.008)	(0.002)	(0.010)	(0.014)	(0.013)
Intensity	-1.637	-0.037*	-0.018	-0.092	0.006	-0.085	0.013	-0.004	-0.128	0.126
	(1.092)	(0.018)	(0.013)	(0.059)	(0.021)	(0.056)	(0.015)	(0.068)	(0.101)	(0.089)
Pubic hair 2	1.576**	0.019	0.000	0.053	-0.003	0.037	-0.020*	0.076*	0.031	0.046
	(0.591)	(0.010)	(0.007)	(0.033)	(0.012)	(0.031)	(0.008)	(0.038)	(0.057)	(0.050)
Pubic hair 3	1.109	0.033*	0.020*	0.063	0.005	0.054	-0.006	0.014	0.066	-0.052
R-squared	0.024	0.576	0.746	0.489	0.382	0.512	0.581	0.316	0.408	0.165
Females										
Magnitude	-4.137*	0.956***	1.008***	1.580***	0.504***	1.655***	0.571***	2.082***	1.887***	0.195
	(1.828)	(0.042)	(0.035)	(0.107)	(0.048)	(0.101)	(0.034)	(0.217)	(0.144)	(0.150)
Timing	0.256	-0.009**	-0.012***	-0.014	-0.002	-0.015	-0.003	-0.022	-0.020	-0.002
	(0.148)	(0.003)	(0.003)	(0.008)	(0.004)	(0.008)	(0.003)	(0.017)	(0.011)	(0.011)
Intensity	0.167	0.073**	0.070***	0.144**	0.020	0.163**	0.033	0.215	0.200**	0.015
	(0.984)	(0.023)	(0.019)	(0.055)	(0.025)	(0.052)	(0.018)	(0.111)	(0.074)	(0.076)
Pubic hair 2	0.309	0.011	0.007	0.017	0.020	0.012	0.015	-0.035	0.009	-0.044
	(0.548)	(0.013)	(0.010)	(0.029)	(0.013)	(0.028)	(0.009)	(0.058)	(0.038)	(0.040)
Pubic hair 3	1.129	0.029	0.015	0.012	0.019	-0.002	0.007	-0.056	0.027	-0.084
	(0.775)	(0.018)	(0.015)	(0.040)	(0.018)	(0.038)	(0.013)	(0.079)	(0.053)	(0.055)
R-squared	0.020	0.633	0.738	0.561	0.341	0.616	0.579	0.371	0.528	0.015

Standard errors in parentheses

*** p<0.001, ** p<0.01, * p<0.05

Table 5-0-4: The timing of the peak velocity of (a) weight gain and (b) BMI gain in relation to age at peak height velocity and their effects on adult body composition and height

(a) adolescent weight gain

	Males			Females		
Adult Variables	**Early**	**Intermediate**	**Late**	**Early**	**Intermediate**	**Late**
N	328	299	276	324	327	327
Range of difference$^{\phi}$ (years)	-8.51: -0.11	-0.11 - 0.38	0.38 - 4.70	-3.09 - 0.36	0.36 - 0.98	0.98 - 4.33
Age peak of height velocity (years)	14.5$^{a***, b***}$ (1.2)	14.2^{c***} (0.9)	13.8 (0.9)	11.9 $^{a**, b***}$ (1.0)	11.7^{c***} (0.8)	11.5 (0.8)
Peak weight velocity (kg/year)	6.9 $^{a***, b**}$ (0.2)	6.8 (0.1)	6.8 (0.1)	6.4^{b**} (0.2)	6.3 (0.1)	6.3 (0.2)
Overweight/obesity (%)	107 (34.5)	109 (34.8)	108 (38.6)	155 (49.7)	206 (53.4)	251 (73.6)
Height (cm)	172.8^{b***} (6.9)	171.6 (6.4)	170.4 (6.4)	161.3^{b***} (6.0)	160.0^{c**} (5.8)	158.3 (6.2)
Weight (kg)	62.9^{b**} (11.4)	60.9^{c***} (9.5)	66.7 (12.1)	61.9^{b***} (17.0)	63.8^{c***} (13.8)	69.7 (16.5)
BMI (kg/m^2)	21.1^{b***} (3.7)	20.6^{c***} (2.7)	22.9 (3.9)	23.8^{b***} (6.4)	24.9^{c***} (5.2)	27.8 (6.0)
Fat mass (g)	13040.0 (6846.9)	11765.2^{c***} (5388.4)	13993.4 (6462.8)	22272.5^{b***} (10127.7)	24055.4^{c***} (9101.5)	28481.1 (9546.9)
Fat-free soft tissue mass (g)	43091.7^{b***} (5577.0)	43592.2 ^{c**} (5768.0)	45831.3 (6206.5)	33128.4 (5424.1)	33512.1 (4865.9)	34240.3 (5058.7)
FMI (kg/m^2)	4.4 (2.3)	3.9^{c***} (1.6)	4.8 (2.1)	8.5^{b***} (3.7)	9.4^{c***} (3.6)	11.5 (3.8)
FFMI (kg/m^2)	14.5^{b***} (1.6)	14.7^{c***} (1.5)	15.8 (1.8)	12.6$^{a*, b***}$ (1.7)	13.2 ^{c**} (1.7)	13.8 (1.7)
Fat mass-to-fat free mass ratio	0.30^{a*} (0.14)	0.27^{c*} (0.10)	0.30 (0.11)	0.66^{b***} (0.22)	0.71 (0.21)	0.83 (0.22)
Visceral adipose tissue mass (g)	468.3 (436.9)	383.4 (311.8)	518.5 (393.6)	1253.2^{b***} (751.4)	1408.7^{c***} (677.9)	1722.3 (691.8)
Subcutaneous adipose tissue mass (g)	217.6 (98.3)	209.1 ^{c**} (92.6)	234.6 (96.4)	239.9^{b***} (168.7)	276.2^{c***} (177.3)	336.4 (174.8)

(b) adolescent BMI gain

Adult Variables	Males			Females		
	Early	**Intermediate**	**Late**	**Early**	**Intermediate**	**Late**
N	328	299	276	324	327	327
Range of difference$^{\phi}$ (years)	-9.92: -1.54	-1.51 - 0.08	0.08 - 8.45	-3.17 - 1.35	1.35 - 2.35	2.35 - 8.11
Age peak of height velocity (years)	14.6$^{a***, b***}$ (1.2)	14.1^{c***} (0.9)	13.7 (0.9)	11.9 ^{b***} (1.0)	11.7^{b*} (0.8)	11.6 (0.8)
Peak BMI velocity (kg/m^2/year)	0.8$^{a*, b***}$ (0.3)	0.9^{c***} (0.3)	1.1 (0.3)	1.4$^{a***, b***}$ (0.3)	1.3^{c***} (0.3)	1.1 (0.3)
Overweight/obesity (%)	83 (25.3)	122 (40.8)	119 (43.1)	232 (71.6)	215 (65.8)	165(50.5)
Height (cm)	172.4^{b*} (6.9)	171.8 (6.2)	170.7 (6.5)	160.5 (6.3)	159.4 (6.1)	159.4 (5.9)
Weight (kg)	59.6$^{a*, b***}$ (8.9)	62.4 ^{c***} (10.4)	69.1 (12.3)	70.7$^{a***, b***}$ (18.3)	64.0 (14.9)	61.7(13.9)
BMI (kg/m^2)	20.0$^{a**, b***}$ (2.7)	21.1 ^{c***} (3.2)	23.7 (3.8)	27.4$^{a***, b***}$ (6.8)	25.2 (5.9)	24.3 (5.2)
Fat mass (g)	11184.8^{b***} (4963.9)	12128.5^{c***} (5968.7)	15518.3 (7061.7)	27386.9$^{a*, b**}$ (11211.1)	24554.8 (9404.1)	23415.9 (8751.6)
Fat-free soft tissue mass (g)	41506.3$^{a***, b***}$ (4805.3)	44165.1^{c***} (5428.5)	47099.5 (6213.7)	34955.9$^{a**, b***}$ (5425.9)	33166.2 (4678.3)	32855.7 (5001.8)
FMI (kg/m^2)	3.8^{b***} (1.7)	4.1^{c***} (2.0)	5.2 (2.2)	10.7^{b**} (4.4)	9.8 (3.8)	9.2 (3.5)
FFMI (kg/m^2)	14.0$^{a***, b***}$ (1.3)	15.0^{b***} (1.4)	16.1 (1.7)	13.6^{b**} (1.9)	13.2 (1.6)	12.9 (1.8)
Fat mass-to-fat free mass ratio	0.27^{b***} (0.10)	0.27^{c***} (0.12)	0.33 (0.13)	0.77^{b*} (0.25)	0.73 (0.22)	0.71 (0.21)
Visceral adipose tissue mass (g)	364.4^{b***} (304.6)	414.4^{c***} (376.5)	593.9 (438.8)	1607.0 (846.0)	1455.1 (644.1)	1356.2 (668.3)
Subcutaneous adipose tissue mass (g)	194.1^{b***} (75.4)	218.1^{c***} (98.4)	251.3 (106.0)	311.5^{b**} (195.9)	281.6 (164.3)	265.9 (169.5)

$^{\phi}$The difference was calculated by subtracting age at peak height velocity from age at peak weight or BMI velocity (e.g. apwv – aphv). This value was categorised by generating tertiles for early, intermediate and late age at peak weight or BMI velocity.

a = early vs. intermediate; b = early vs. late, c = intermediate vs. late

*p < 0.05, **p < 0.01, ***p < 0.001

Chapter 6 Patterns of Obesity and Their Effect on Linear Growth

6.1 Background

This chapter addresses questions which have been raised through findings from the published chapters of this thesis. Data from this thesis seem to suggest that black females experience less growth faltering than black males, despite being exposed to the same adverse environment throughout the growth period. Black males had the highest prevalence of stunting, and it appears that there was a greater disparity in growth percentiles for height between black and South African white males and the international reference, compared to what was observed in females. In addition, during adolescence black males experienced an 8-month delay in the attainment of age of peak height velocity which was 3 months earlier in females. The difference in peak height velocity between black and white males was also larger than that observed in females. Given that black females had a similar BMI magnitude but a faster velocity of BMI gain than white females in adolescence, leading to a higher prevalence of overweight and obesity, a question arose whether linear growth among black females could be buffered by adiposity. This was informed by the hypothesis which suggests that adiposity accelerates linear growth, such that heavier children tend to be taller than lean children at a given age.

This hypothesis has been supported by findings from a HIC which showed that childhood BMI was associated with taller childhood height but not adolescent height. The authors did not assess the relationship with adolescent weight. Data testing this hypothesis in settings where there is a high prevalence of both under- and overnutrition are scant. Given the existence of the double

burden of malnutrition which has been demonstrated in this thesis and the potential role of adolescence as a window of opportunity to influenced adult height, there is a need to assess these patterns through adolescence.

Lastly, this thesis investigated the association between the timing of the onset of overweight and obesity and adult body composition and the risk of obesity. This is informed by evidence which show that early onset obesity has been associated with greater adult BMI. However, data from this thesis have shown that the effects of the timing of weight and BMI gain are contradictory and sexually dimorphic. In females, attaining age of peak weight velocity (APWV) before age of peak height velocity (APHV) was associated with lower BMI and fat mass while the reverse was true for age of peak BMI velocity (APBV). In contrast to females, males who attained APBV earlier than APHV had lower BMI and fat mass than those who attained it later. prevalence of obesity rises sharply during adolescence in females. Thus, the objectives of the additional analyses were to investigate:

- The age-related changes in the prevalence of underweight from early childhood to early adulthood
- The age-related changes in height deficit between black and white males and females?
- The effect of adiposity on height deficit in black males and females
- The effect of the timing of the onset of overweight/obesity on adult body composition and the risk of obesity

6.2 Results

6.2.1 Prevalence of Underweight

There were racial and sex differences in the prevalence of underweight (***Figure 6-1***). At age 2 years, the prevalence was higher among black children and lowest among white males. In late childhood, black females had an over 5% higher prevalence than black males, but this was reversed during adolescence with black males having a consistently higher prevalence.

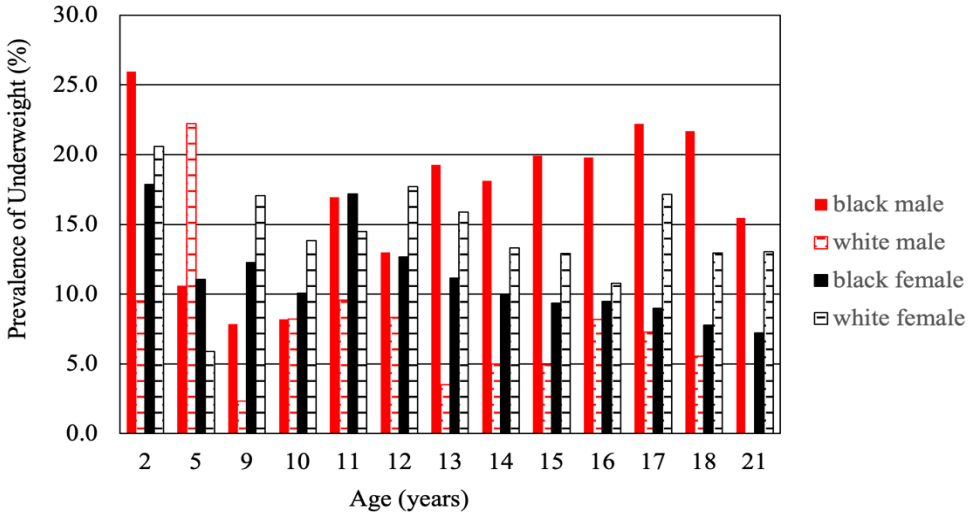
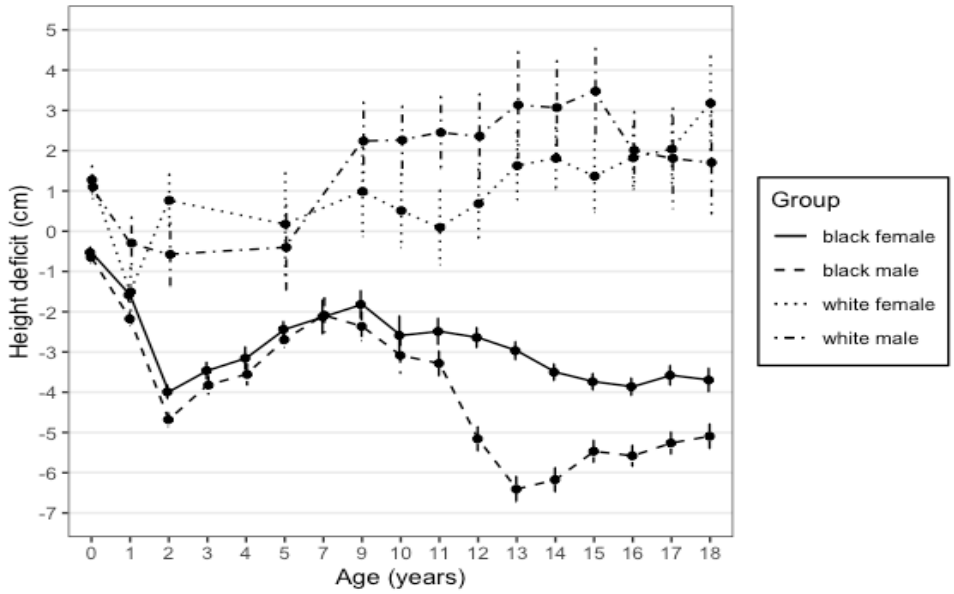


Figure 6-1: Prevalence of underweight for black boys (red solid), white boys (red dashed), black girls (black solid), and white girls (black lines)

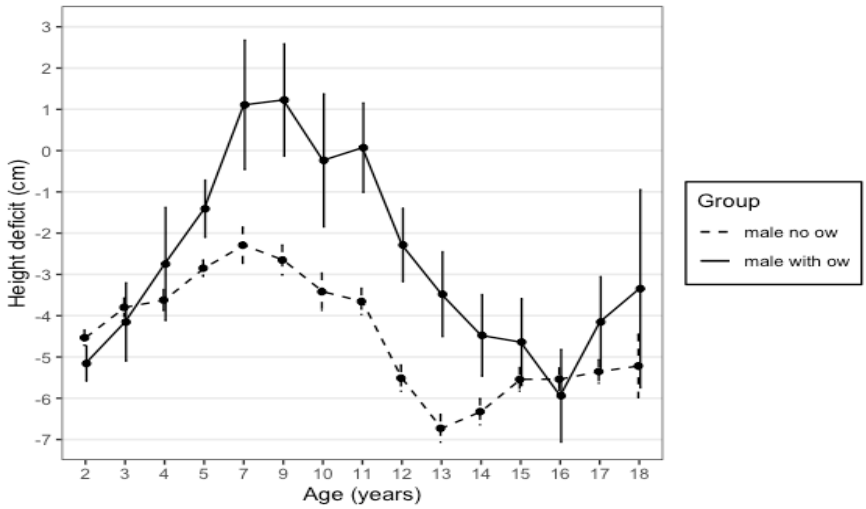
6.2.2 Effect of Obesity on Linear Growth

Black boys experience a wider deficit than black girls, which is absent in white children. Additionally, black boys experience a 1 cm (from -6.3 to -5 cm) improvement in height deficit from the age of 13 years (***Figure 6-2***). This improvement is earlier in boys with no obesity (13 years) than boys with obesity (16 years). Among black children, those with overweight/obesity experienced a lower height deficit and delayed widening of the deficit compared to children with no overweight/obesity in both sexes.

(a)



(b)



(c)

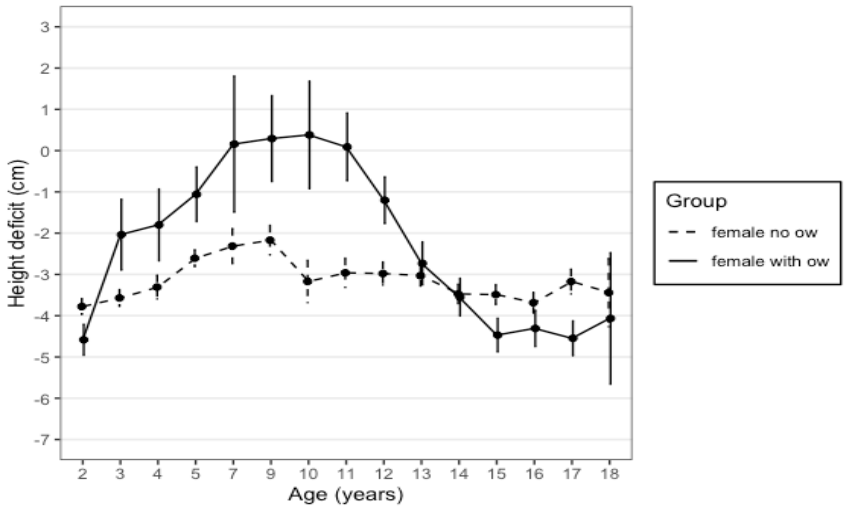


Figure 6-2: Changes in height deficit over time between (a) black and white children, (b) black males with vs those without overweight/obesity, and (c) females with vs those without overweight/obesity

6.2.3 Timing of the Onset of Obesity and Adult Body Composition

Early (childhood and early adolescence) onset overweight/obesity was associated with greater odds of adult overweight/obesity and greater parameters of adiposity in both males and females (***Table 6-1***). Pattern 1 is never overweight/obese at any stage (NNN); pattern 2 is late adolescence onset overweight/obese (NNO); pattern 3 is early adolescence onset and persistent overweight/obese (NOO); and pattern 4 is childhood onset and persistent overweight/obese (OOO). N=never, O= overweight/obese

Table 6-1: Differences in adult body size and body composition among overweight/obese individuals according to patterns of onset of overweight and obesity during three stages of development, childhood (0 – 8 years), early adolescence (9 – 13 years) and late adolescence (14 – 17 years).

Adult outcomes	**Females**				**Males**			
	Pattern 1	**Pattern 2**	**Pattern 3**	**Pattern 4**	**Pattern 1**	**Pattern 2**	**Pattern 3**	**Pattern 4**
N (overweight/obese)	524 (117)	215 (96)	129 (106)	106 (99)	623 (41)	200 (34)	67 (39)	48 (35)
% Overweight/obese	22.3	44.7	82.2	93.4	6.6	17.0	58.2	72.9
Odd Ratio (ref: pattern 1)		2.8 (2.0 – 3.9)	16.0 (9.8 – 26.3)	49.2 (22.3 – 108.8)		2.9 (1.7 – 4.7)	19.8 (11.1 – 35.3)	27.6 (14.4 - 52.9
Height (cm)	158.8 (5.2)	158.8 (6.1)	158.8 (5.9)	159.7 (6.1)	171.1 (7.4)	171.0 (5.8)	169.8 (6.8)	172.0 (7.3)
BMI (kg/m^2)	27.7 (2.5)	29.0 (3.6)	32.0 (5.8)	34.0 (6.2)	27.2 (2.1)	27.6 (2.7)	28.4 (4.3)	30.0 (5.3)
Waist circumference (cm)	86.4 (8.5)	89.6 (10.6)	94.2 (13.9)	96.8 (13.3)	87.3 (7.6)	87.2 (9.8)	89.6 (10.9)	95.8 (13.6)
Waist-to-hip ratio	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.8 (0.0)	0.9 (0.1)
Fat mass (g)	28.5 (5.7)	31.1 (7.3)	34.9 (9.1)	37.3 (10.5)	21.6 (6.6)	21.6 (5.6)	22.3 (6.9)	25.0 (8.0)
% Body fat	43.9 (4.5)	45.5 (5.1)	46.1 (5.5)	47.3 (5.2)	28.7 (6.1)	28.3 (5.5)	29.4 (5.7)	31.5 (7.5)
% Trunk fat	40.3 (6.1)	41.7 (6.3)	42.9 (7.2)	44.2 (6.1)	26.4 (7.0)	26.4 (6.3)	27.1 (6.2)	29.6 (8.3)
FMI (kg/m^2)	11.3 (2.1)	12.4 (2.8)	14.0 (3.7)	14.5 (3.5)	7.3 (2.2)	7.4 (1.9)	7.7 (2.3)	8.4 (2.6)
FM/FFM ratio	0.8 (0.2)	0.9 (0.2)	0.9 (0.2)	1.0 (0.2)	0.4 (0.1)	0.4 (0.1)	0.4 (0.1)	0.5 (0.2)

Chapter 7 Overall Discussion and Conclusion

7.1 Summary of Objectives and Key Findings

Table 7-1: Summary of findings from the thesis

Objectives	Chapter	Summary of key findings
To assess age-related changes in the prevalence of overweight, obesity and growth, and to compare their percentiles between race groups with international reference values.	**3**	• Black boys had the higher prevalence of stunting, underweight and wasting than black girls and white boys. • Black girls had a higher prevalence of overweight and obesity than white girls and black boys. • Height percentiles of black children were lower than those of South African white and CDC references. • Weight and BMI percentiles of black females were similar to those of South African white and CDC references. • Waist circumference percentiles of black and white South African females were lower than NHANESIII references.
To characterise racial differences in height, weight and body mass index (BMI) during adolescence.	**4**	• White children were 5 cm (SE: 0.7) taller than black children during adolescence • APHV was 0.65 years (SE: 0.12) later in black than white boys • APHV was 0.24 years (SE: 0.11) earlier in black than white girls. • Black girls had 16% faster BMI velocity than white girls during adolescence and early adulthood

To assess the association between early childhood growth and the magnitude, timing, and intensity of adolescent growth.	**4**	• Early childhood growth explains the variance in adolescent BMI, weight and height by ~20, ~30 and ~50%, respectively. • Higher birth weight and rapid linear growth from birth to 5 years were associated with greater adolescent height • Higher birth weight and rapid weight gain from birth to 5 years were associated with a higher adolescent BMI • Rapid weight gain from birth to 5 years was associated with an earlier timing of gain in adolescent BMI
To assess the association between the magnitude, timing and intensity of adolescent growth, and young adult body composition.	**5**	• Greater weight during childhood was associated with an earlier onset of puberty, a greater intensity of weight gain in adolescence, and a resurgence of weight gain in early adulthood • When APBV occurred earlier than APHV, it was associated with greater early adult BMI, whole-body fat mass, FMI and subcutaneous adipose tissue in females, but the reverse was true in males
To assess: Age-related changes in the prevalence of underweight from early childhood to early adulthood Age-related changes in height deficit between black and white males and females? The effect of adiposity on height deficit in black males and females The effect of the timing of the onset of overweight/obesity on adult body composition and the risk of obesity	**6**	• Black females had a higher prevalence of thinness in the peripubertal period (9 to 10 years of age) • Black males had a higher prevalence of thinness during adolescence • Black males experienced a greater height deficit than black females • A 1 cm improvement in the height deficit was observed during adolescence in black males • Black children experienced growth faltering in infancy and late childhood in males • Childhood weight status was associated with taller concurrent height but not this was not true during adolescence and in early adulthood • Childhood onset overweight and obesity was associated with greater BMI, whole-body and abdominal FM

This chapter is a summary of the key objectives, hypotheses and findings of the studies included in this thesis, and the strengths and limitations of this thesis. The contextual relevance of the salient findings and how they pertain to future research are outlined. The chapter concludes with a discussion on the contribution of this thesis to our understanding of growth in South African children.

Hypotheses

There were four hypotheses (H) which were tested in this thesis. The response (R) to each hypothesis is given below the hypothesis:

5. H: White children are taller and heavier than black children.

   R: White children were 5 cm taller than black children of both sexes, and white males were heavier than black males. The hypothesis is accepted

6. H: Black males have a delayed timing of the adolescent growth spurt for height and age of peak height velocity

   R: Black males experienced an 8-month delay in APHV. The hypothesis is accepted

7. H: A greater magnitude, earlier timing and higher intensity of adolescent weight and BMI are associated with greater adult BMI and whole body and abdominal fat mass

   R: The magnitude, intensity (both positively associated), and timing (negatively associated) of adolescent weight and BMI explain between 30 and 80% of the variance in adult BMI, FM, FFM, FMI, VAT and SAT. The hypothesis is accepted

8. A later timing of adolescent height gain is associated with taller adult height.

R: When magnitude and intensity are accounted for, an earlier timing of height growth is associated with taller adult stature in females. The hypothesis is rejected.

This thesis has three empirical chapters which addressed the objectives set above. Chapter 3 is a descriptive chapter and gives context to the growth of urban South Africa children in relation to SES, using racial comparisons, as well as comparison to international references. South Africa has a heterogenous social and economic structure, which is primarily determined by race, as a legacy of the apartheid system (296). The percentiles presented in this chapter provide a reference population to which future studies can be compared. This is the first novelty of this thesis. The percentiles from this thesis could be used as a reference to assess whether changes in percentiles of future samples are driven by a shift in a sub-sample or the whole population. Studies in the US have shown that the secular change in BMI was influenced by a widening of the centile lines among those who were in the higher percentiles (237). Although this thesis did not investigate temporal changes in height and weight, the high prevalence of overweight and obesity among black females suggests that there has been a rise in weights of black females overtime. Historically, South African children were both shorter and lighter and had lower adipose tissue compared to children from HIC (55,236). Data from this thesis show that although black children are still shorter, the average weight and BMI of black females is now similar to growth percentiles for South African white children and international references. This is another novel finding. Notwithstanding, they still have smaller waists and hips, possibly due to the shorter average height.

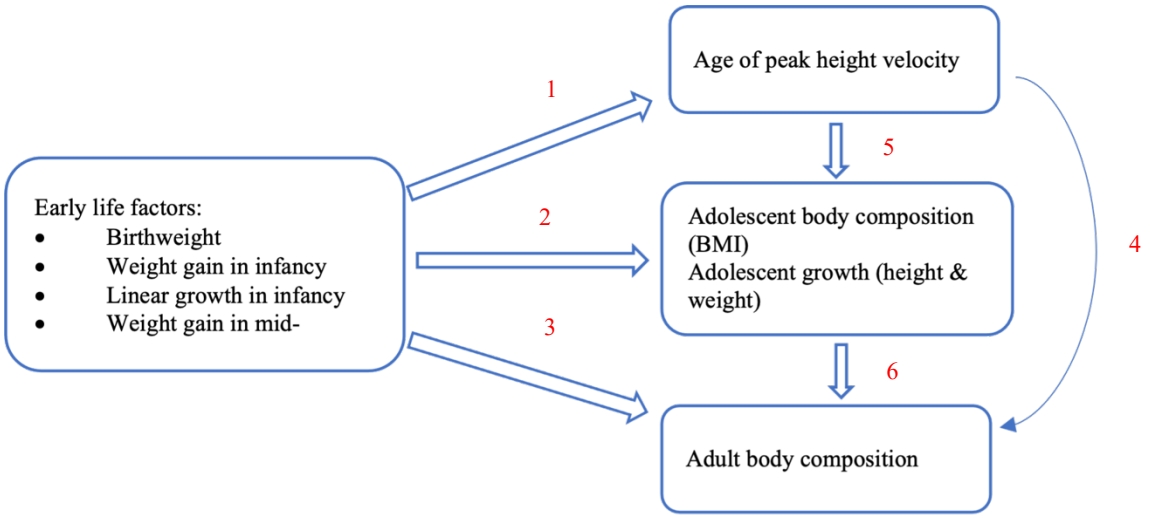


Figure 7-1: Original conceptual framework applied to this thesis

The empirical questions raised in the conceptual framework of this thesis are addressed in chapter 4 and 5. The original conceptual framework applied to this thesis proposed several pathways to demonstrate the effect of childhood growth, puberty, and adolescent growth on adult body composition. Not all pathways were fully tested in this thesis. The thesis characterised the growth of children from the Bt20+ cohort and described the magnitude, timing, and intensity of the adolescent growth spurt in height, weight, and BMI. The novelty of this thesis is the characterisation of the adolescent growth spurt for BMI. The pathways in the conceptual framework which were investigated were paths 1, 2, 4, 5 and 6. The thesis did not investigate path 3 and the combination of paths 1 & 4, and paths 1, 5, & 6.

In chapter 4, this thesis tested the associations between early childhood growth and the magnitude, timing, and intensity of adolescent growth for height weight and BMI. The association of early childhood growth with APHV can be inferred from the associations with the timing of height as APHV is derived from the timing, and the two have a correlation coefficient

of 1. The findings show that only rapid linear growth between birth and 5 years was associated with an earlier APHV in boys. In females, both rapid linear growth and rapid weight gain between birth and 5 years were associated with an earlier APHV. Notwithstanding, the associations with both rapid weight gain and rapid linear growth between 2 and 5 years were weaker than with associations between birth and 2 years. Rapid weight gain between 2 and 5 years was associated with shorter adolescent height, while rapid linear growth between birth and 5 years was associated with taller stature. Paradoxically, rapid linear growth between birth and 5 years was associated with heavier adolescent weight and earlier weight gain but not BMI in both sexes. Higher birth weight and rapid weight gain between birth and 5 years were associated with heavier BMI. The positive association between rapid linear growth and weight raises the question about the desire to promote linear growth in this age group and in these settings.

In chapter 5, this thesis investigated paths 4, 5, 6 and the combination of path 5 and 6. The timing of height and therefore APHV was negatively associated with all measures of adult body composition, affirming path 4 of the conceptual framework. Taller adolescent height was paradoxically associated with greater FM and FFM in both sexes, and FMI in males. The magnitude of weight and BMI, and rarely the intensity of weight were significant predictors of adult body composition. Thus, weight attained and less so the rate of weight gain during adolescence is a key determinant for adult body composition, affirming path 6 of the conceptual framework. When assessed in reference to biological maturity (APHV), an earlier timing of BMI gain was associated with greater adult BMI, FM and FMI in females. By modelling height and weight and stratifying by the pubertal development trajectories for pubic hair, this thesis examined the effect of puberty on the magnitude, timing, and intensity. During adolescence,

there were differences in the magnitude, timing, and intensity but the differences in magnitude disappeared in adulthood for height, while they remained for weight. Earlier developers appear to have experienced a post adolescent acceleration in weight gain. This affirms path 5 of the conceptual framework

Lastly, the additional results in chapter 6 confirm the buffering of black females against growth faltering. They experienced a smaller height deficit than black males, who experienced additional growth faltering in late childhood. However, black males experienced an improvement of about 1 cm in height during adolescence, suggesting that there may be some residual plasticity during adolescence for influencing adult height. Additionally, the results confirm the persistence of early onset overweight and obesity, in childhood and early adolescence, and its detrimental effects on adult body size and composition. The findings give insight into the importance of the timing of intervention for obesity. Secondly, the findings show that adiposity provides a buffer against growth faltering, although the effects disappear in adolescence, affirming the hypothesis that adiposity accelerates linear growth (297), in childhood.

7.2 Emerging themes

There are three main themes which emanate from this thesis, and they are discussed in the context of local and international studies. The themes are: (i) additional periods of growth faltering among black children & residual plasticity, (ii) understanding the covariance of height and weight during childhood – implications for association analyses, and (iii) the rise in weight and BMI growth velocity in late adolescence in females.

7.2.1 Additional period of growth faltering among black children

This thesis highlights significant differences in height between black and white children, and in the timing of the adolescent growth spurt between black and white males. Using height deficit, this thesis showed that black children experienced greater height deficits than white children, and black boys than girls. There was an increase in deficit between birth and 2 years of age, a pattern which is similar to that demonstrated using HAZ (34,219). Similarly, to HAZ, which show and improvement between 2 and 5 years, there was a narrowing of the deficit (improvement in sample mean height) which extended to about the age of 9 years in black children. Rodriguez et al showed that the heights of children from LMIC reached optimal height by age 5 years, but progressively fell behind the WHO references as they approached age 19 years of age (298). Data from this thesis show that black males experienced a further widening of the deficit after age 9. However, there was an improvement in the height deficit with black boys experiencing a 1 cm rise in height during adolescence, suggesting the presence of residual plasticity. Whether these periods of growth faltering are independent or act cumulatively to entrench growth faltering among black males as they enter puberty is unclear.

The findings point to systemic drivers of undernutrition and that upstream interventions are required to reverse stunting in South Africa. The experience of early childhood adversity is common among South African children with 65% of black children living in households where income falls below the upper-bound poverty line compared to 31% of Coloured, 16% of Indian and 3% of white children (299). Consequently, food insecurity is common in South Africa with

30% of children (largely black) in 2002 living in households where they reported to go hungry "sometimes", "often" or "always" due to food shortage (300). Data from the Bt20+ cohort have shown inadequate energy intakes among black and Indian infants compared to their Coloured and white counterparts (301). The authors showed that black children had the lowest consumption of macronutrients compared to the other race groups (301), and their consumption of micronutrients such as calcium, iron, zinc, vitamin A, riboflavin, nicotinic acid, pantothenic acid and biotin was lower than the recommended daily allowance (RDA) (302).

South Africa has experienced a mix of successes and failures in addressing maternal and child health. The country has one of the highest rates of health coverage on the continent, with 97% of births attended by skilled health personnel and 96% of deliveries happening at a heath institution (299). The public health budget as a percentage of GDP has increased only marginally from about 3.5% to just over 4% between 1994 and 2017. With regards to basic services, the biggest improvement was observed for clean cooking techniques and electricity which rose by over 20%, with over 80% of the population having access to these resources in 2017 (303). Access to clean water and proper sanitation has also improved, rising from 55 to just below 70% in a 26-year period. Notwithstanding these improvements, persistent poverty, and high unemployment may mitigate against drastic reductions in the prevalence of undernutrition.

Additionally, rapid urbanisation among the black population may increase their vulnerability to poor health outcomes. South Africa has been experiencing rapid urbanisation coming from a low baseline, with just over 50% of the population being urbanised in 1990 (304). While an urban environment, with better infrastructure, may have significant advantages over a rural

environment, factors such as the rise in informal housing may be detrimental for child growth. Migration to Soweto, which is a suburban area in Johannesburg, South Africa, where the Bt20+ cohort resided, was described as "economically disequilibrating" in that "it did not close the income gap that triggered the migration process in the first place" (305).

7.2.2 Covariance of height and weight during childhood

Findings from this thesis show that rapid linear growth was associated with an earlier APHV and heavier adolescent weight and BMI. This presents a paradox as there is a desire to improve linear growth in childhood, in order to improve adult height and human capital (34). This thesis suggests that rapid linear growth could mask the covariance of height and weight in this period, given the impact of adiposity on linear growth demonstrated in this thesis. Early childhood growth was assessed using conditional relative weight (CRW) and conditional length (CL), which are generated to address the issue of collinearity between height and weight. The computation of CRW accounts for present length while the computation of CL does not account for present weight (261). Data from this thesis provide evidence which supports the hypothesis that overnutrition accelerates linear growth (306,307). Studies which report a positive association between preadolescent BMI and GH binding protein (308) and serum growth factors which influence linear growth (IGF-1) (309) underscore the potential role of adiposity on growth. He and Karlberg found that childhood BMI was positively associated with concurrent height but negatively associated with adolescent height and not associated with adult height (285). This underscores the covariance of height and weight in childhood and potentially the need to account for concurrent weight in association studies for linear growth.

Adiposity could underscore the sexually dimorphism observed in racial differences in height in this cohort. Black females had a lower height deficit from WHO 2007 growth references (5 to 19 years) and had similar weight, BMI, and earlier timing of APHV with South African white females. The differences in peak height velocity were greater in males (8.7 vs 10.6 cm/year) than females (7.3 vs 7.7 cm/year), in black and white adolescents respectively. Black males also experienced an 8-month delay in the attainment of APHV than white males while it was 3 months earlier in black than white females. The peak velocity for height in black children is similar to that of children from a pastoralist, hunter-gathering society (Tsimane) in Mexico who had peak velocity of 8.8 cm/year for boys and 8.2 cm/year for girls (256) but notably lower than that observed in British males (10.3 cm/year) and females (9.0 cm/year) (310).

The delay in APHV in black males in this study corroborates the findings of a 6-month delay in skeletal maturity in black males compared to their white counterparts but not in females during puberty in this cohort (189). These patterns have also been shown between Senegalese and British adolescent, where Senegalese males experienced a 1-year delay in APHV compared to British males, which was not observed in females (262). Several hypotheses have been employed to explain this sexual dimorphism. Cole et al attributed the delay in skeletal maturity in black males to male susceptibility to stress (189). This hypothesis suggests that males are less buffered from environmental insults and their growth and maturation may be more adversely affected than that of females (311). Males and females also respond differently to intervention, with improvements in heights of females but not in males (312).

7.2.3 Adolescent weight gain and the rise in weight and BMI velocity in early adulthood

Findings for this thesis show that sex and racial differences in BMI occurred in adolescence. Black females had a higher velocity of BMI gain in adolescence than white females, leading to a higher prevalence of overweight and obesity in mid-adolescence and early adulthood. Sex hormones play a key role in the normal accrual and distribution of fat and lean tissue during adolescence, with testosterone promoting muscle gain in males, and oestrogen influencing gain in fat mass in females (61,174). However, behavioural factors may be the biggest drivers of the disparity in adiposity between black males and females. A previous Bt20+ study showed low levels of physical activity among black adolescents (313). Urban black women displayed higher sitting times and lower amounts physical activity than urban black men and rural black women (314), possibly linked to safety concerns among urban women (315).

In addition to poor levels of exercise, a proliferation of fast food and sugar-sweetened beverage outlets in South African townships may promote unhealthy eating habits. A study of the distribution of advertising and vendors of sugar-sweetened beverages and fast-foods in Soweto showed their proximal location to schools, which contributes towards increased uptake of these items by school-going children *(**Figure 7-2***) (316). The “kota”, a quarter load of bread with various fillings (***Figure 7-3***), was the most popular choice of fast-food due to its affordability and filling ability and has a high caloric content (317). Fast-food consumption was high among the Bt20+ participants with more than two-thirds of the cohort consuming fast foods and sugar-sweetened beverages at least three times per week, whilst more girls consumed confectionary at least seven times per week than boys (247).

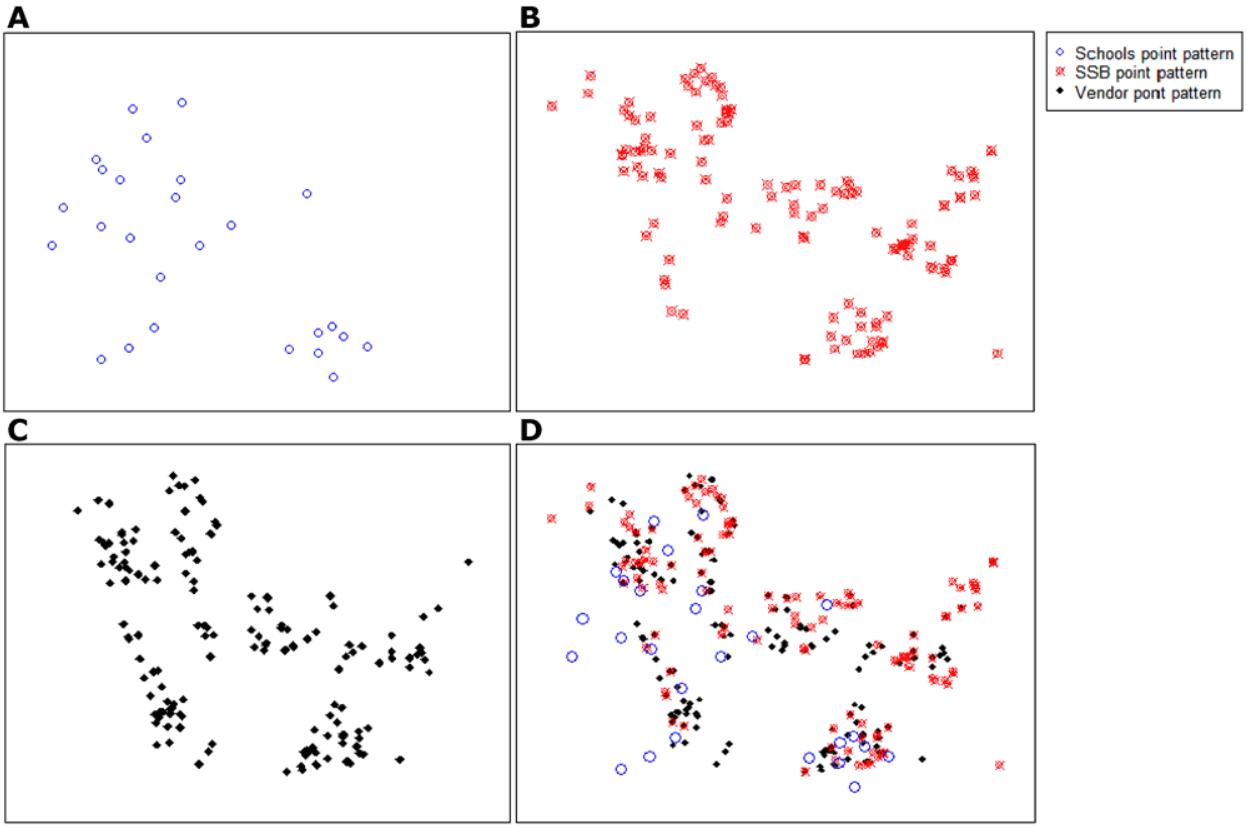


Figure 7-2: Distribution of schools and vendors and advertisement for sugar-sweetened beverages. The dots present locations of schools (a - blue), sugar-sweetened beverage (SSB) vendors (b - red) and SSB outdoor advertising (c - black). The three locations were superimposed in the last panel (d). Source: Moodley (316)

Figure 7-3: The most popular fast food in Soweto, South Africa (317)**. The "kota" is a quarter loaf of bread with various fillings but most commonly, fried potato chips, fried eggs, and cheese. Source: webpage** (318)

In addition to adolescence, early adulthood is another critical period for the development of obesity in South African black females. Black females experienced a resurgence in the velocity of weight and BMI gain in early adulthood, following a decline in late adolescence. This resurgence was higher among those who were heavier in childhood. They had an earlier onset of puberty, a greater magnitude of BMI in adolescence and a resurgence of weight gain in young adult females. It is suggested that the period 18 to 25 years of age represents a period of greater weight gain than any other period in the lifecourse (168). The transition to early adulthood is associated with unhealthy eating habits and reduction in physical activity (168) as teenagers leave high school where they participated in organised sport. However, concurrent physical activity was a significant determinant of early adulthood fat mass only in males while childhood total body and trunk fat mass were the most important contributors in females (319).

7.3 Implications of the findings of this thesis

This thesis has several conceptual and methodological implications; (i) the potential of dual patterns of the obesity epidemic driven by socio-economic status as indicated by race, (ii) the presence of growth faltering in black males in the late childhood/prepubertal period and the role of adiposity in influencing linear growth, (iii) the resurgence of weight and BMI velocity in early adulthood in black females, and (iv) applicability of SITAR in modelling body composition.

Firstly, the use of race in nutritional epidemiological studies has been questioned (320,321). Race does not confer biological properties or advantage but in the context of South Africa, it is an important proxy for residential location and socio-economic status. South Africa is experiencing multiple transitions, with not only increasing urbanisation, but also movement from lower socioeconomic urban areas to more affluent suburbs. It would be interesting to assess whether there are race differences in the nutritional transitions among individuals residing in similar suburbs and having a comparable socio-economic standing. Several transitions may be responsible for differences in the patterns of obesity in low and high income societies (322).

Secondly, the thesis also highlights another potential critical period for growth faltering. Growth faltering has previously been shown to occur predominantly in early childhood with catchup growth and maintenance from mid-childhood to adulthood. This thesis shows growth faltering among black boys that occurs in the prepubertal period. There is a need to understand factors associated with this decline. The widening deficit was observed in both those with and without

obesity in males but only among those without obesity in females. Adiposity accelerates linear growth in childhood, although the benefit disappears in adolescence. Notwithstanding, black females maintain a lower height deficit throughout the growth period, possibly due to factors associated with the rise in obesity in females.

Thirdly, black women experience a resurgence in the velocity of weight and BMI in late adolescence and early adulthood. The rise is faster among those who were heavier in childhood. Thus, management of weight in childhood among females may be key in influencing the trends in adult obesity. Thus, improving nutrition and physical activity among school-going girls from as early as primary school may influence the trajectories of growth by delaying the onset of childhood adiposity, with positive effect on the timing of puberty, the magnitude of adolescent weight and BMI gain, and the velocity of weight and BMI gain in late adolescence.

Finally, this study has shown the usefulness of using SITAR to study growth patterns of multi-ethnic South African children. The SITAR random effects of magnitude, timing and intensity are exportable and provide a summary of the growth characteristics for each individual. These parameters can be utilised in future studies that investigate malnutrition in South Africa.

7.4 Future research

Ideas for future research which flow directly and indirectly from the findings of this thesis are presented below:

1) Mediating effect of puberty timing and adolescent body size on the association between early childhood growth and adult body composition

The thesis fell short of assessing the full path of the conceptual framework that informed it. Further studies could assess whether the association between early childhood growth and adult body composition is mediated by puberty and adolescent growth. Findings by Stein at al indicated that puberty and childhood body size could jointly determine adult BMI. This has not been investigated in relation childhood growth rate and to the components of BMI, fat mass and lean mass.

2) Factors associated with growth faltering in late childhood

The second study arising from the findings of this thesis is understanding the drivers of growth faltering in late childhood in black children and whether this is associated with earlier growth faltering.

3) Individual Risk Score for Obesity

The Bt20+ cohort is the first, largest and longest running cohort of child health in Africa. Data from this thesis have provided insight into some of the risk factors associated with malnutrition. The value of cohort studies lies in the ability to collect individual information on exposures and outcomes, which can assist in teasing out key factors associated with risk. To date, although population level analyses have been performed, they have not been translated into individual risk scores for health outcomes. This thesis and other studies on the cohort have generated individual data which describe their growth trajectories and can be used to develop an individual risk score, in a similar fashion to the Framingham risk score for coronary heart disease (323). This could be a useful tool for public health education and intervention. With the rise in machine learning skills, the individual trajectories and raw data may be used to further develop algorithms for predictive analyses.

4) Understanding drivers of behaviour among young girls

South African black females have a higher risk of developing obesity and this risk is established in childhood. Early childhood intervention in needed to prevent childhood obesity. The uptake of sport and physical activity is lower among black females while the consumption of unhealthy foods is higher. Studies elsewhere have demonstrated the low effects of adult exercise intervention in females. There has been no focused intervention which targets females, to assess factors associated with early onset obesity. A cohort where young girls between 4 and 11 years can be randomised into different arms of intervention and control, and followed up in an

accelerated longitudinal design study could provide insight into the prevention of obesity among females.

7.5 Strengths and limitations

This thesis has several strengths and limitations. The strength of this thesis is the use of all the available data to model the longitudinal growth and to develop the percentiles for height, weight, and BMI. This provided the best available sample for the analyses ensuring sufficient power for the modelling. Secondly, the use of SITAR to model the data is compatible with the longitudinal nature of the data. To this end, there was no need for imputation of missing data as the model is built to handle missingness. Thirdly, the use of SITAR to model the data provides useful parameters which summarise the data in exportable and biologically interpretable parameters which can be used in further studies as exposures or outcomes to test hypothesis. Associations with early childhood growth were assessed using conditional growth measurements, which are based on regression residuals to address the collinearity of height and weight values. However, concerns have been raised about the use of unexplained residuals as they artificially reduced estimated standard errors (324). Disaggregating the analyses by race as well as biological sex has allowed for multi-ethnic comparisons across different populations which give insight into the effect of ecological factors of development. The analyses were adjusted for confounding factors. However, the study also had limitations. The analyses were not adjusted for feeding patterns and nutrient intake. Only intermediary measures of health outcomes were assessed, and the thesis did not investigate the effect of the different growth patterns on markers of cardiometabolic disease.

7.6 Concluding Remarks

This thesis used a lifecourse development approach to address two important global health problems which are plaguing LMIC, the persistently high prevalence of undernutrition and the emerging obesity pandemic. There are additional periods of growth faltering and residual plasticity in black children. Thus, there are several windows of opportunity to influence growth: 1) in foetal/infancy and prepubertal periods to promote optimal linear growth, 2) childhood to early adolescence to prevent unhealthy and persistent body mass gain, and 3) late adolescence to prevent and resurgences in weight and BMI velocities in women. Long-term obesity could have more adverse effects for cardiometabolic disease risk.

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