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Body Mass Index Trajectories: The Effect of Fetal Size and Early Life Modifiable Factors

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Epidemiology and Biostatistics

BODY MASS INDEX TRAJECTORIES: THE EFFECT OF FETAL SIZE AND EARLY LIFE MODIFIABLE FACTORS

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by

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Abstract

Background: This study examined the relationship between small for gestational age (SGA) status at birth, a measure of fetal growth restriction, and childhood body mass index trajectories (BMI) using data from the National Longitudinal Survey of Children and Youth. Analytic Method: Using latent growth curve modeling, the growth trajectories of a cohort of small and appropriate for gestational age singletons were modeled from 2-10 years (N=1,273 at baseline). Results: SGA status had no effect on the growth trajectories of children after adjusting for prenatal and early life sociodemographic and maternal variables, and also early life modifiable factors. Moreover, the modifiable factors (physical activity, sedentary screen time and sleep duration) had no effect on childhood BMI. Conclusion: The findings of this study do not lend support to the fetal origins hypothesis, which state that adaptations to adverse conditions in utero results in increased risk of disease in later life.

Keywords

fetal growth, growth restriction, small for gestational age (SGA), childhood, obesity, body mass index (BMI), latent growth curve modeling (LGCM), life course, time-varying covariates, National Longitudinal Survey of Children and Youth (NLSCY)

Dedication

I dedicate this thesis to my parents,
Roy Philip Kurian and Raichel Roy,
and my brother, Philip Roy.

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I would like to thank Dr. Piotr Wilk for providing me with a great deal of guidance and assistance throughout the last two years. Dr. Wilk's mentorship, together with his pragmatic approach and sense of humour has made my graduate experience a positive one. I would also like to express my sincere gratitude to Dr. Karen Campbell for offering her expertise and constructive input, which has allowed me to present to a sound piece of work.

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List of Abbreviations

AGA	Appropriate for Gestational Age
BIC	Bayesian Information Criterion
BMI	Body Mass Index
CCHS	Canadian Community Health Survey
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
FIML	Full Information Maximum Likelihood
HPA	Hypothalamic-Pituitary-Adrenal Axis
IGF-1	Insulin-Like Growth Factor
IOTF	International Obesity Task Force
IUGR	Intrauterine Growth Restriction
LFS	Labour Force Survey
LGA	Large for Gestational Age
LGCM	Latent Growth Curve Modeling
MAR	Missing At Random
MCAR	Missing Completely At Random
N	Sample Size
NPHS	National Population Health Survey
OR	Odds Ratio
PMK	Person Most Knowledgeable
RR	Relative Risk (Risk Ratio)
SGA	Small for Gestational Age
SES	Socioeconomic Status
SEM	Structural Equation Modeling
WHO	World Health Organization

Chapter 1

1 Introduction & Literature Review

1.1 Introduction

Obesity is a disease characterized by excess fat mass, and is a substantial contributor to the burden of disease worldwide. Obese individuals are at risk for many health conditions, including diabetes, coronary heart disease, stroke, high blood pressure, sleep apnea, osteoarthritis, and many cancers.[1] This results in a decrease in health-related quality of life and overall life expectancy.[2]

The prevalence of obesity has increased to epidemic levels in Canada and around the world. The World Health Organization (WHO) reported in 1999 that there were approximately 250 million obese people in the world, and that this number would rise to 300 million by 2025.[3, 4] A more recent report has shown that the prevalence has far surpassed this prediction, to approximately 500 million obese people in 2008.[5] At a societal level, obesity has considerable costs that strain our healthcare and social resources. In Canada, the 2006 direct medical cost of overweight and obesity was $6.0 billion.[6]

This trend of increasing obesity prevalence is particularly concerning since obese children are more likely than normal weight children to develop diabetes, high blood pressure, asthma, depression, and poor self-esteem.[1] Also, it has been shown that obese children are likely to be affected by many of these chronic conditions in adulthood, because they are more likely to become obese adults.[7]

Public health efforts aimed at controlling childhood obesity has had limited success due to the multifactorial nature of obesity.[2] Particularly, there is still much to learn about the effects of prenatal and early life factors on obesity risk.

One area of research, which is important for the development of targeted prevention strategies for childhood obesity, relates to the potential fetal origins of later disease development. The fetal origins hypothesis (also referred to as the programming or thrifty

phenotype hypothesis) suggests that insults during critical stages of fetal development, most commonly fetal malnutrition (indicated by a small size at birth), results in metabolic programming of the fetal genome and changes to physiological functions and structures (in order to aid fetal and postnatal survival). It further states that if postnatal life is followed by nutritional abundance, this will result in increased risk for obesity and other chronic diseases later in life.[8-10]

Despite its history, the fetal origins hypothesis remains contentious. Evidence in favour of the fetal origins hypothesis has been criticized for deficiencies in study methodology, improper control for confounders, and conflicting results.[11] The majority of studies that have examined the effect of small size at birth on childhood obesity have failed to account for socioeconomic factors. This certainly may have confounded the association between size at birth and later obesity. In addition, many have used low birth weight rather than small for gestational age as a measure of growth restriction. Low birth weight as a measure of growth restriction does not fully capture those who are growth restricted (see Section 1.3.2). Moreover, many studies on this topic have been cross-sectional in nature, and as a result may have failed to account for factors occurring between the exposure and outcome. Thus, it is not possible to conclude that a causal relationship exists from these studies alone. To overcome this problem, this study places the emphasis on growth trajectories throughout childhood rather than obesity status at a single age. By doing so, factors occurring through childhood can be accounted and more information regarding the trajectory of growth and overall child health can be gained.

Research on the link between fetal origins (or small size at birth) and obesity have relied on an approach that is mainly biological. Because childhood obesity depends on patterns of growth through early life, a life course framework is necessary when exploring the link between small size at birth and early childhood weight trajectories. In the context of chronic disease epidemiology, the life course approach is the study of long-term effects of physical and social exposures from gestation to adulthood on chronic disease risk.[12-15] This study takes such a broader approach by taking into account socioeconomic conditions in childhood and examining the influence of factors in early life such as

physical activity, sedentary behaviours, and sleep duration on growth trajectories of children.

The following section will review the current evidence on obesity (Section 1.2), including the trends in childhood obesity (Section 1.2.1), its health effects (Section 1.2.2), how it is currently defined (Section 1.2.3), and factors associated with obesity risk (Section 1.2.4). The next section describes fetal growth restriction and its measures (Section 1.3) and factors that lead to growth restriction (Section 1.3.1). This is followed by a description of the fetal origins hypothesis and fetal growth as a predictor of obesity (Section 1.3.2). This includes an explanation of the proposed biological mechanisms and an analysis of the current evidence on the fetal origins of obesity. Section 1.3.3 describes the life course perspective and how factors such as catch-up growth, diet, physical activity, sedentary behaviours, and sleep duration affect weight status in children.

1.2 Obesity

1.2.1 Prevalence of Obesity

In Canada, the prevalence of obesity in youth aged 12 to 17 years has almost tripled from 3% in 1978-1979 to 9% in 2004.[16] These figures are from the Canadian Community Health Survey (CCHS) which used the International Obesity Task Force (IOTF) cut-offs to classify overweight and obesity.[17] Results from the CCHS shows that in 2004, 26% of Canadian children and youth aged 2 to 17 years were either overweight or obese, while 8% were obese.[16] Similar figures were also reported in the 2009-2011 Canadian Health Measures Survey (CHMS) in 6 to 17 years olds. Based on IOTF cut-offs, in 6 to 17 year olds, the rate of overweight and obesity was 24.8%, while the rate of obesity was 8.4%.[18] Reports from this survey also suggest that increases in BMI over time were a result of increased adiposity, rather than muscularity.[19]

Rates of obesity also differed significantly between boys and girls of 6 to 17 years when the World Health Organization (WHO) cut-off was applied.[20] The rate of obesity in boys was 15.1%, while in girls this number was 8.0%. In the subgroup of 5 to 11 year olds, this difference was even more apparent, with a 19.5% rate of obesity for boys and 6.3% for girls.[18]

These findings are concerning since weight gain in the early years of life often continues into adulthood and because health issues that arise from childhood obesity are sometimes not evident until later in life. These concerns highlight the importance of focusing more on the early years of life and the need for strategies that prevent disease development later in life.

1.2.2 Health effects of obesity

Obesity is well recognized as an inflammatory disease; therefore, many of the consequences of obesity stem from systemic inflammatory responses.[21] In conjunction with hypothalamic-pituitary-adrenal axis (HPA axis) activation as a result of genetic susceptibility and environmental stressors (ex. nutritional overload, stress, sleep etc.), the resulting hormonal and metabolic abnormalities contribute to the development of later disease.[22] Overweight and obese children are more likely than normal weight children to exhibit risk factors for chronic disease. Such risk factors include abnormally elevated lipid and insulin levels, low HDL cholesterol levels, and high blood pressure. Childhood obesity and accompanying risk factors can persist into adulthood leading to disease development later in life.[19, 23, 24] Obese children are at 25 to 50% greater risk of becoming obese adults.[23] Diseases that have been consistently shown to be associated with obesity include Type II Diabetes, coronary artery disease, congestive heart failure, hypertension, stroke, asthma, gallbladder disease, osteoarthritis, colorectal cancer, and postmenopausal breast cancer. Diseases resulting from childhood obesity are also emerging earlier in life. In particular, Type II Diabetes is also becoming more common in children as result of increasing obesity rates.[19, 23, 24] Besides the physical consequences, childhood obesity also effects mental health. Obese children are more likely to experience discrimination by their peers, and to have lower self-esteem and body image.[19, 24]

1.2.3 Defining Obesity

Though methods exist to directly measure the amount of fat in the body, they are complicated, expensive, and not easily accessible.[25] Instead, indirect methods based on weight and height are used to define obesity. A common measure used to define obesity

is body mass index (BMI), which is weight in kilograms divided by height in metres squared.

In adults, definitions of overweight and obesity have been established using absolute BMI cut-offs associated with increased risk of morbidity and mortality. In children however, a higher BMI is not associated with a greater incidence of morbidity or mortality, because weight-related diseases are less prevalent a younger age.[23] The major approach to identify overweight and obesity in children has been developed by the Centers for Disease Control and Prevention (CDC). Using, BMI-for-age growth charts for males and females, the CDC defines healthy weight, overweight, and obesity as having a BMI between the 5th and the 85th percentile, 85th percentile and the 95th percentile, and greater than the 95th percentile respectively.[26]

One limitation of solely relying on such cut-offs is that they do not reveal the actual risk of developing obesity related diseases, as risk may also be dependent on the presence of other factors such as size at birth, rapid weight gain in early life, physical activity levels, and dietary patterns.[24] Thus, a single figure describing obesity status does not reveal much about health when compared to growth patterns from birth throughout childhood. Thus, it is more important to consider growth patterns along with early factors of childhood growth than obesity status at a single age.[27]

1.2.4 Factors associated with obesity risk

Obesity develops over a long period of time as the result of an imbalance between energy intake (through consumption of fat, carbohydrates, and protein) and energy expenditure. While obesity is generally caused by excess energy consumption (dietary intake) in comparison to energy expenditure (loss off energy through metabolic and physical activity), it is a multifactorial disease. Obesity involves genetic, physiological, environmental, psychological, and sociodemographic factors that act in conjunction to promote disease development.[25, 28]

An issue with determining if a factor is causal or not is that it is difficult to establish temporal precedence due to problems in establishing the onset of the disease. However,

risk factors occurring in the prenatal and postnatal periods can be concluded to precede the onset of the obesity. Thus, more research into this area can uncover information about the factors related to the etiology of obesity. The primary focus of this study is on fetal growth restriction as a leading factor for obesity, and this will be discussed more in-depth in Section 1.3. Before doing so, the following is a review of factors that have been shown to be associated with obesity development.

Ethnicity

The effect of ethnicity on obesity has not been fully explained in literature, but many studies have reported that South Asians are at greater risk for obesity.[29-34] Studies have also shown that Hispanic and African-American children are also at greater risk. In a nationally representative sample of American children and adolescents born in the early 1990s, Hispanic and African-American children were more likely to have accelerated patterns of weight gain compared to White and Asian children.[35] Similar results were found in other large scale studies.[36, 37]

Maternal age

Conclusive evidence regarding the association between maternal age and obesity risk remains to be seen. There is some indication that increased maternal age is associated with increased obesity risk in offspring (independent of birth weight). One study of 1,739 participants showed that, a maternal age greater than 30 years is not associated with obesity trajectories in children from two to twelve years of age (OR=2.7, 95% CI: 1.0 to 7.2). Adjustments were made for birth weight, sex, race, birth order, gestational age, breastfeeding, maternal pre-pregnancy BMI, maternal weight gain, smoking and alcohol use during pregnancy, maternal age at the birth of the child, mother's education level, and family net income.[37] However, another study of 5,156 American children from a national longitudinal survey showed that compared to mothers 20 to 24 years of age, those who were born to mothers over 25 years were less likely to be obese in adolescence (10-18 years) (adjusted for prenatal, demographic, and familial factors) ($OR_{25\text{-}29}$ years=0.92, $p<.01$; $OR_{30\text{-}34}$ years=0.89, $p<.01$). This association remained even when birth weight was taken into account.[38]

Parity

Prior studies have shown a modest association between primiparity and risk of childhood obesity. One retrospective study of 8,904 children reported that first-born children have a greater risk of obesity (BMI $\geq 95^{th}$ percentile) from 2 to 5 years compared to those who were not first-borns (OR=1.34, 95% CI: 1.11 to 1.62). This study also adjusted for size at birth, gender, ethnicity, maternal age, marital status, maternal education, maternal BMI, maternal smoking, and weight gained during pregnancy.[39] Another study of 945 children reported that children of primiparous mothers were heavier and taller than children of multiparous mothers from 1 year and onward.[40]

Maternal Smoking

Studies have consistently shown a small association between maternal smoking and increased obesity risk in offspring. In a recent review by Behl et al. (2013), 34 of 42 studies supported a causal relationship between maternal smoking and childhood overweight and obesity.[41] Another meta-analysis of 16 studies also found that maternal smoking during pregnancy was associated with obesity risk (BMI $\geq 95^{th}$ percentile) (pooled adjusted OR=1.52, 95% CI: 1.36 to 1.70).[42] Similar results were also found in another meta-analysis of 14 studies by Oken et al. (pooled adjusted OR=1.50; 95% CI: 1.36 to 1.65).[43] Likewise, the Quebec Longitudinal Study of Child Development (N=1,957) reported that maternal smoking was associated with high-rising BMI trajectories as compared to low-stable and moderate rising BMI trajectories (OR=2.28, 95% CI: 1.49 to 4.04).[44]

Maternal Hypertension

Reports on the association between maternal hypertension and obesity in the offspring are very limited and conflicting. The Raine study of 1,197 Australian children, followed up from birth to 14 years, identified 8 different adiposity trajectories, among which includes a ‘lifelong high adiposity’ trajectory comprising children who were above 1 z-score for adiposity. Among other factors, this trajectory was associated with an increased rate of maternal hypertension.[45, 46] In their investigations, Kuhle et al. (2011) and Ehrenthal et al.

(2013) did not find any association between maternal hypertension and obesity risk. [47, 48] Both adjusted for maternal and socioeconomic factors, while the study by Kuhle also adjusted for childhood factors such as physical activity levels and screen time.

Maternal Diabetes

The link between maternal diabetes and greater obesity risk in offspring is questionable. Studies of the Pima Indian population have shown that obesity is more common among children of diabetic pregnancies regardless of birth weight.[49, 50] A sibling study of Pima Indian offspring (six to twenty-four years of age) confirmed that children of mothers who had diabetes during pregnancy had significantly higher BMI when compared to siblings born to mothers who did not have diabetes ($p=0.003$).[51] However, this relationship can be at least partially explained by maternal BMI. A recent review of seven epidemiologic studies reported that there was a positive association between maternal gestational diabetes mellitus and offspring overweight and obesity (crude OR: 1.2 to 2.8). However, of the six studies that adjusted for pre-pregnancy BMI, this association was significantly attenuated (though four still showed a modest association, ORs ranged from 1.6 to 2.3).[52] A cross-sectional study of 14,881 American adolescents, also reported that being born to a mother with gestational diabetes was associated with increased odds of being obese (BMI $\geq 95^{th}$ percentile) (OR=1.4, 95% CI: 1.1 to 2.0). However, after adjusting for birth weight and maternal BMI (along with other lifestyle factors), the association was no longer statistically significant (OR=1.2, 95% CI: 0.8 to 1.7).[53]

1.3 Fetal growth restriction

Fetal growth restriction also referred to as intrauterine growth restriction (IUGR) is the failure of a fetus to reach its biological growth potential due to an underlying pathological process.[54, 55] Growth restricted infants have a higher risk of perinatal and infant mortality, and morbidity. They have a perinatal mortality rate that is 10 to 20 times higher than who are not growth restricted.[56] Growth restricted infants also have higher rates of hypertension, cardiovascular disease, diabetes, renal in-sufficiency, and impaired reproductive function. These children are also prone to neurological impairment and delayed cognitive development.[9, 54, 55, 57]

Due to difficulties in measuring fetal growth, small for gestational age (SGA) is the most commonly used measure of intrauterine growth restriction. A SGA infant is one with a birth weight less than an expected cut-off, for a given gestational age and sex.[57, 58] The most widely used cut-off is a birth weight less than the 10th percentile for gestational age and sex.[58] However, SGA is not synonymous with growth restriction, since an infant may be SGA as a result of being constitutionally small.[58, 59]

From 1995-2008, the rate of SGA among singleton live births in Canada decreased from 10.1% to 7.8%,[60, 61] and increased slightly from 8.1% in 2008-2009 to 8.7% in 2011-2012.[62] In 2011-2012, this accounted for approximately 32,000 hospital births. The overall decrease in SGA rate can be attributed to increases in the birth weight distribution as a result of increases in maternal size, reduced cigarette smoking, changes in sociodemographic factors and increased gestational dating accuracy (due to wider use of ultrasound technology).[61]

1.3.1 Factors associated with fetal growth restriction

Ethnicity

Black and South Asian mothers are at greater risk for a SGA birth. A case-control study of 2,478 children from singleton births showed that Black ethnicity was associated with SGA after adjusting for chronic hypertension, pre-gestational diabetes, illicit drug use, and advanced maternal age (>35 years).[63] Another study based on singleton births reported that Asian-Indian mothers had a higher risk of term SGA births compared to White mothers (OR=2.98, 2.92 to 3.05). This study also found that African-American mothers also had a higher risk for term SGA birth (OR=2.29, 2.21-2.37). The study adjusted for marital status, maternal age, maternal educational attainment, parity, nativity of mother, prenatal care utilization, diabetes, and hypertension.[64] A study from New Zealand showed that Indian ethnicity was associated with increased risk for SGA (OR=3.22; 95% CI: 1.95 to 5.30) after adjustment for other maternal and prenatal factors. No significant association was found between European, Maori, Pacific, Chinese, and other ethnicities and SGA.[65] Also, in a review of the determinants of low birth weight,

Kramer stated that Black, Indians, and Pakistanis have lower birth weights than European and North American Whites.[66]

Maternal age

Maternal age only has a small effect on the risk of being born SGA. Studies on this topic have reported odds ratios that are trivial. A hospital based cohort study of 65,280 singletons without major congenital anomalies delivered between 1978 and 1996 showed that maternal age ≥35 years was associated with greater odds of being born growth restricted at term compared to maternal age between 20-34 years. However, the odds ratio was very close to one (OR=1.13, 95% CI: 1.03 to 1.24). Adjustments were made for maternal education, marital status, primiparity, maternal height, pre-pregnancy BMI, net maternal weight gain (minus infant birth weight), pre-pregnancy hypertension, pregnancy-induced hypertension, diabetes (pre-pregnancy or gestational), and maternal smoking.[67] Similarly, a case-controlled study also showed that compared to a maternal age <25 years, a maternal age of ≥25 years was associated with greater odds of being born SGA (25-34 years: OR=1.74, 95% CI: 1.18 to 2.56; >34 years: OR=1.98, 95% CI: 1.08 to 3.64). This study also took into account maternal obesity status, employment status, race, smoking status, drug use, perceived health status, systolic blood pressure, preeclampsia, and rhesus positive blood type.[68]

Parity

Maternal parity has a small influence on size at birth. Evidence from a study of 945 children shows that children of primiparous pregnancies were lighter, shorter, and had smaller head circumferences, and were also thinner (lower ponderal index) at birth compared with other infants.[40] Another systematic review of 14 cohort studies also linked primiparity with greater odds of SGA when compared to multiparous mothers (pooled adjusted OR=1.80, 95% CI: 1.62 to 2.01).[69]

Maternal Smoking

The most important and modifiable cause of fetal growth restriction is maternal smoking.[70] Smoking in pregnancy is a significant preventable risk factor for an adverse pregnancy outcome. Smoking exposes the mother and the fetus to a variety of harmful compounds that cause fetal hypoxia and growth restriction.[70, 71] Nicotine, carbon monoxide, and the metabolite cotinine are just a few of the compounds that are passed on to the baby through the placenta.[72-74] Causal epidemiological data shows that tobacco use by mothers leads to a 70 to 250 gram reduction in birth weight.[74]

Kramer (1987) concluded that smoking-related reduction in birth weight is mediated primarily by fetal growth restriction.[66] Literature consistently shows a dose-response relationship and reduction in effects of smoking with cessation.[75-77] A systematic review found that the risk of having an SGA child is 1.5 to 3 times greater in mothers who had smoked during pregnancy. Another study of 782 SGA and 827 AGA term infants, found that maternal smoking was associated with two-fold increase in the risk of an SGA baby. This association remained significant after adjustment for ethnicity, occupation, age mother left school, marital status, marijuana use, parity, age of mother at first pregnancy, age of mother at the present pregnancy, maternal height, maternal pre-pregnancy weight and maternal hypertension, gender, gestational age (adjusted OR=2.4, 95% CI: 1.78 to 3.28).[65] In regards to smoking cessation, a recent Cochrane review of 72 studies showed that smoking cessation interventions reduced the risk of low birth weight (RR=0.83, 95% CI: 0.73 to 0.95) and increased mean birth weight by approximately 54 grams (95% CI: 10.44 g to 95.38 g).[78] Another study also showed that smoking cessation by 15 weeks gestation can reduce the rate of SGA, such that it is similar to that of non-smokers.[79] The differences observed in effect sizes between observational studies and smoking cessation studies might be related to other behaviours exhibited by smokers that were not controlled for in these studies.

Maternal Hypertension

Many reports have shown that hypertension (pre-gestational and gestational) is associated with increased risk of being born SGA.[75] Similar to smoking during pregnancy, maternal

hypertension leads to fetal hypoxia and ultimately growth restriction.[71, 80] A retrospective cohort study by Gilbert et al. found that women with chronic hypertension had greater odds of having growth restricted infants (OR=4.9, 95% CI: 4.7 to 5.2). Compared to mothers without chronic hypertension, the risk of having a child with low birth weight was also very high (OR=5.4, 95% CI: 5.2 to 5.5).[81] The greater risk for SGA was also independent of pre-eclampsia, a condition of the placenta characterized by high blood pressure, rapid weight gain, and protein in the urine. Similarly, a cohort study consisting of 560,188 women aged 15-44 years with singleton pregnancies found that women with chronic hypertension have a higher risk for a SGA child (OR=3.1, 95% CI: 2.7 to 3.7), after adjusting for many maternal factors. After introducing superimposed pre-eclampsia, the association still remained (OR=2.4, 95% CI: 2.1 to 2.9)[82] A Canadian study of 135,466 pregnancies in Nova Scotia found that women with pre-existing hypertension also had a higher risk for an SGA birth (RR=2.5, 95% CI: 2.1 to 2.9). Women with gestational hypertension without proteinuria (a condition in which the urine contains abnormal amount of protein) were almost two times more likely to have a live birth with SGA (OR=1.8, 95% CI: 1.7 to 1.9).[83] One study reviewed, however, did not find any link between hypertension during pregnancy and small size for gestational age.[47, 54, 84]

1.3.2 Fetal growth restriction as a predictor of obesity

Babies born small at birth have a greater risk for the development of cardiovascular diseases and metabolic syndrome later in life.[9] The 'fetal origins of adult disease' hypothesis states that adverse influences or insults in utero, programs permanent changes in physiology and metabolism, which result in disproportionate fetal growth and increased risk of disease in later on.[8]

In 1992, Hales and Barker proposed the thrifty phenotype hypothesis, which states that under conditions of malnutrition, delivery of nutrients to the body and organs is restricted in favour of nourishment of the brain. This reprogramming of the fetal physiology and metabolism occurs in a manner that optimizes survival for conditions of poor nutrition after birth.[9] When there is a "match" between the expected and the actual environment, the infant confers protection from future disease and survival is maximized.[85] However, when there is a mismatch between the environments and the infant is subjected to

conditions of adequate nutrition, fetal programming may result in the development of metabolic diseases.[9]

Biological Mechanisms

Research on the relationship between SGA and later obesity shows that any relationship between the two may occur independently of a predisposing genotype.[10] A recent study of gene variants associated with obesity has found that non-genetic or environmental factors may be more important than genetic factors in influencing BMI in SGA children.[86] The mechanisms underlying the associations between small size at birth and obesity and remain unclear. However, several have been proposed. Specifically, changes to the insulin and insulin-like growth factor (IGF-1) axis, and the HPA axis are implicated in disease development.

One proposed mechanism states that stressful intrauterine conditions lead to activation of the HPA axis and abnormally high levels of cortisol and glucocorticoids. The rise in glucocorticoids levels is intended to be beneficial because it results in higher levels of glucose and other sources of energy for the fetus. However, overexposure can have lasting effects on the cardiovascular system, including changes to the HPA axis' response to feedback hormones, and changes to renal morphogenesis and the renin-angiotensin system. Excess glucocorticoid levels also reprogram enzymes of the liver, resulting in permanent up-regulation of glucose production. This results in decreased insulin sensitivity and increased insulin resistance later in life. Overexposure to cortisol levels also results in alterations to cell growth, leading to irregular growth patterns and possible negative consequences after birth.[10, 87]

Alterations to the glucose-insulin-IGF-1 axis have also has been implicated in fetal programming. Reduced availability of nutrients results in reduction of IGF-1 and insulin levels, ultimately leading to restricted fetal growth. This is speculated to occur in order to salvage vital organs (i.e. brain) at the cost of growth. However, this response becomes a liability after birth due to nutritional abundance (i.e. high levels of insulin and IGF-1 due to adequate nutritional supply) which leads to obesity and insulin resistance.[10, 87]

Evidence for the link between growth restriction and childhood obesity

Associations between size at birth and obesity were originally shown in historical cohorts. In a study of a cohort born between 1911 and 1930 in Hertfordshire, England, low birth weight individuals had a greater risk of death from cardiovascular disease and stroke.[88] Studies of those who were born during the Dutch winter famine of 1944-1945 have also shown that undernourished women gave birth to children who were smaller at birth, who subsequently developed obesity, insulin resistance, hypertension and coronary artery disease in adulthood.[89]

Studies that are more recent have also shown similar results. In an eight year cohort study of 851 term SGA and AGA subjects, SGA subjects had a greater gain in BMI, an indicator of obesity, in adulthood than AGA individuals (SGA: 1.8 kg/m^2 vs. AGA: 1.4 kg/m^2, p=0.03). This study also found that at 30 years of age, more SGA individuals were obese (BMI $\geq$ 30 kg/m^2) (12.1% vs. 6.5%. p=0.02). Similarly, the waist circumference gain was significantly greater in SGA subjects after adjustment for age and gender (6.4 cm vs. 5.5 cm, p=0.04).[9] Similar results were found in another cohort study of 3,148 individuals. It was found that SGA was an important predictor of abdominal obesity (waist-hip ratio $\geq 90^{th}$ percentile) at age 31 in men (OR=2.00, 95% CI: 1.34 to 2.98), after adjustment for maternal age, and maternal BMI before pregnancy. These results have also been replicated in experimental animal models. Rat pups who were subject to restricted fetal growth (as a result of maternal food restriction) had lower birth weights and increased body weight and body fat as adults.[89]

Despite such reports, the link between growth restriction (SGA) and later disease remains controversial. Evidence supporting the fetal origins hypothesis has been criticized for use of low birth weight as an indicator for fetal growth restriction, improper control for confounders, and design deficiencies.

The majority of studies that have examined the fetal origins of obesity have used low birth weight, defined as a birth weight of less than 2,500 grams as an indicator of growth restriction. However, there are severe limitations to its use for such examinations. First, low birth weight may result from fetal growth restriction, pre-term birth, or both. Since

pre-term birth and growth restriction are associated with different pathologies and health outcomes, it is difficult to ascertain the determinant of the low birth weight.[57, 90] Thus, the use of low birth weight as an indicator can lead to opposite trends in pre-term and growth-restricted births being masked. Secondly, a recent study from low- and middle-income countries has shown that most growth restricted neonates (~64%) weigh more than 2,500 grams at birth.[90, 91] So, the use of low birth weight to identify growth restricted infants fails to identify most children who are truly growth restricted.

Another criticism of the observed association between small size at birth and later obesity regards the lack of adjustment for socioeconomic status. It is known that low socioeconomic status (SES) is a common determinant of poor fetal growth and small size at birth, unhealthy diets, smoking, lack of physical activity, and later obesity. Thus, absence of control for SES can lead to residual variation and improper conclusions about the fetal origins of later disease. Though, a few studies that have controlled for SES found that the association with later disease remained,[92-95] and one reported that it was strengthened after adjustment.[96, 97] However, another study reported that the association was no longer significant after adjusting for SES.[98]

Moreover, many of the studies that have analyzed the effect of small size at birth on obesity have focused on outcomes as an adult, and those that have focused on children have used varying ages for outcome evaluation. These studies also use different definitions for small size at birth and obesity status. In addition, the cross-sectional nature of studies may have led to erroneous conclusions because of the potential to miss important aspects of the relationship during the unobserved periods. To overcome these issues, this study places the emphasis on growth trajectories throughout childhood rather than obesity status at a single age. This allows for the observation of patterns of growth and the identification of trajectories at risk for weight related disorders. The influence of other variables on such patterns of growth can also be assessed by utilizing trajectories.

1.3.3 Life course perspective: factors through the life course that may modify obesity risk

The life course approach is defined as "the study of long-term effects of physical and social exposures during gestation, childhood, adolescence, young adulthood, and later adult life on chronic disease risk".[12, 13] It integrates both biological and social factors throughout life to study their contribution to later disease risk. If indeed small for gestational age children have greater risk for obesity, it is of great importance to identify factors after birth that may modify this risk. Thus, this study will also look at how early life factors effect growth trajectories. The identification of such factors will help public health efforts with reducing the risk of childhood obesity.

Catch-up growth

Investigation of the fetal origins of later obesity using the life course framework necessitates consideration of the effects of 'catch-up growth', which is characterized by accelerated growth (rapid gain in body weight) in early life. Many studies have reported that postnatal catch-up growth may modify the effect of intrauterine influences on later disease.[13, 99] The catch-up growth hypothesis states that this tendency to experience rapid catch-up in growth is a result of the body's natural response to intrauterine growth restriction and nutrient deprivation. Though catch-up growth may occur at any stage of growth, most SGA infants will catch-up during the first two years of life.[9, 40]

Evidence on the effect of catch-up growth on SGA infants, however, is still inconclusive. Several studies have shown that SGA and low birth weight infants who have undergone catch-up growth are more likely to have greater central adiposity and lower lean mass.[100-108] In contrast, one systematic review of 21 studies found that there was no interaction between catch-up growth and weight at birth in their effect on obesity and concluded that the effects of rapid weight gain do not differ between SGA and AGA populations.[109]

Dietary Intake, Physical Activity & Sedentary Behaviours

In the life course perspective, lifestyle factors such as time spent performing physical activity and sedentary behaviours are important as they contribute to energy balance. The idea behind energy balance is straightforward. When the amount of energy intake (consumption) exceeds energy expenditure, there will be a positive energy balance. If this surplus persists, it will lead to weight gain. Three factors that contribute to the idea of energy balance and weight gain are dietary intake, physical activity, and sedentary behaviours.

Dietary intake

Certainly, diet plays a large role in weight gain. The rise in energy consumption levels over the past three decades has also seen with it a rise in obesity prevalence.[110] Experimental studies have shown that excess dietary fat and carbohydrate intake leads to weight gain.[111] Many observational studies have also found a link between fatty food consumption, decreased meal frequency, and bigger portion sizes with weight again in children.[23, 112-114] Moreover, low intakes of fruits and vegetables have been associated with childhood obesity risk. Results from the 2004 CCHS show that those who consume less than 5 servings of fruits and vegetables per day are at much greater risk of being overweight or obese than children consuming more than 5 servings.[24] The rise in unhealthy dietary patterns demands an increase in energy expenditure to prevent overweight or obesity. Two ways of doing so are by increasing physical activity levels and by reducing sedentary behaviours.

Physical Activity

The Canadian Society of Exercise Physiology recommends that children 1-4 years old should accumulate at least 180 minutes of physical activity at any intensity throughout the day, and that children ages 5-11 years should accumulate at least 60 minutes of moderate to vigorous-intensity physical activity daily. Reports from the 2009-2011 Canadian Health Measures Survey show that 84% of 3-4 year olds in Canada meet the

physical activity recommendations, but only 7% of 5-11 year olds and 4% of 12-17 year-olds meet the guidelines.[115]

There is moderate evidence for a link between lack of physical activity and obesity risk. A review by Ortega et al. (2008) reported that physical fitness levels are associated with abdominal and total obesity.[116] Data from the European Youth Heart Study (EYHS), a school-based, cross-sectional study of 9–10 years olds showed that those who participated in vigorous physical activity had significantly lower total adiposity as measured by skinfold thickness (adjusted for age, sex, and study location).[117] These results were also replicated in 15-16 year olds when body fat was measured by Dual Energy X-ray Absorptiometry.[116, 118-120] The AVENA study, a large cross-sectional study of 2,859 Spanish children ages 13 to 19 years found that moderate to high levels of cardiorespiratory fitness are associated with lower abdominal adiposity.[116, 121] A cohort study of 4,550 children also reported that BMI increased at a rate 0.05 unit/year slower for children who participated in outdoor organized team sports at least twice per week compared with children who did not. Comparable rates were also found in children who participated in non-school related structured activities.[122] Also, in the Framingham Children's Study, compared to active children, preschool-aged children with low levels of physical activity gained significantly more subcutaneous fat.[100, 123]

Sedentary behaviours (TV/Computer use)

Due to its contribution to decreased energy expenditure, sedentary screen time is strongly associated with increased obesity risk. It is also associated with the consumption of fatty snack foods and this contributes to an increase in energy intake.[124, 125] Results from the 2009-11 Canadian Health Measures Survey showed that only 18% of 3-4 year olds and 69% of 5-11 year olds adhere to the recommended daily screen time (less than 1 hour of screen time for 3-4 year olds, and no more than 2 hours for 5-17 year olds). Presently, 3-11, and 12-17 year olds spend approximately 2.3, and 3.5 hours per day on screen-based sedentary behaviours, respectively.[115]

In adults, there is strong evidence to show that sedentary behaviours are associated with dysfunctional lipoprotein regulation, increased body mass, and a greater risk of

cardiovascular disease and mortality.[115, 126-129] Literature consistently describes a link between screen-based sedentary behaviours and negative health outcomes in children and youth. Longitudinal studies reveal a positive association between self-reported television viewing and BMI.[115, 129, 130] A cohort study of 1,037 individuals reported that the effects of watching too much television in childhood persist into adulthood. Those who spent more hours watching television in childhood had a higher BMI by 32 years of age. This study controlled for sex, childhood socioeconomic status, early BMI, and parental BMI.[131] An intervention study of 192 third and fourth grade students (mean age of 9 years) assessed the effects of reducing television, videotape, and video game use on changes in body composition. The study found that compared to controls, children in the intervention group had a significantly lower BMI (adjusted BMI difference = -0.45 kg/m^2, 95% CI: -0.73 kg/m^2 to -0.17 kg/m^2).[132] Similar trends are also seen with computer use. A study of 460 adolescents (mean age 15 years) found that those who used computers on weekdays more than 4 hours per day were much more likely to be overweight or obese (OR=5.79, 95% CI: 1.79 to 18.69).[133] Another study of 2,560 adults found that compared to those who did not use computers during their leisure time, those who did were more likely to be overweight or obese (even if they were highly active during majority of their leisure time) (OR=1.70, 95% CI: 1.07 to 2.72).[134]

Sleep duration

Sleep plays an important role in the growth, maturation, and health of children. Many mechanisms have been put forth that describe the relationship between sleep and obesity. One theory states that changes to the sleep stages as a result of lack of sleep leads to fatigue, daytime sleepiness, somatic and cognitive problems, and low activity levels and energy expenditure. Other theories state that lack of sleep results in changes in levels of several hormones, leading to increased appetite, and food intake leading to overweight or obesity.[135-137] Wells et al. (2011), in their meta-analysis concluded that a sleep duration of less than 10 hours is enough to increase the odds of obesity by 89%.[138] In their meta-analysis, Chen et al. (2008) found that those with shorter sleep duration had much greater odds of being overweight or obese (pooled OR = 1.58, 95% CI: 1.26 to 1.98). In children, this risk was 92% greater.[135] In another review by Liu et al. (2012) all 25 studies

considered found that short sleep duration is significantly associated with an increased risk of overweight and obesity.[139] Evidence also shows that short sleep duration as early as 6 months of age is associated with greater risk of being overweight or obese later in life.[131, 139] Many studies have also found a dose-response relationship between sleep duration and risk of overweight and obesity in children less than 10 years old.[100, 135]

Though most existing evidence suggests that shorter sleep duration affects weight, some suggest that sleep problems can also result from excessive weight or metabolic disorders. Therefore, caution is still required when considering the direction of causation in the sleep-obesity association.[138, 139]

1.4 Summary

With childhood obesity prevalence on the rise, it is becoming more important to understand its prenatal origins. Though many studies show a relationship between growth restriction (or SGA) and obesity, past research is limited by use of poor indicators of growth restriction, design deficiencies, lack of control for confounding factors, and use of weight status at a single age. This study takes the next step in studying the effects of small size at birth on childhood obesity trajectories by addressing some of these limitations. By using term SGA in contrast to low birth weight as an indicator of growth restriction, more growth restricted children can be identified. Additionally, by utilizing a longitudinal design rather than a cross-sectional one, factors occurring over the growth period can be accounted for, temporality of exposures can be established, and cohort effects are no longer problematic. Also, by using such a design, the focus can shift from obesity status at a one point in time to growth trajectories throughout childhood. Doing so allows for the identification of the patterns of growth and provides more understanding of overall child health. This project also applies a life course framework to the study of the fetal origins of disease. This includes the examination of how other social and biological factors affect growth trajectories. If childhood obesity risk is significantly influenced by prenatal and early life factors, this has implications for public health efforts.

Chapter 2

2 Objectives and Hypotheses

2.1 Objectives

Objective 1:

To assess whether BMI trajectories from 2 to 10 years differ between children born appropriate for gestational age (AGA) and small for gestational age (SGA) at term. Trajectories in children born large for gestational age (LGA) will not be examined.

Objective 2:

To assess whether the effect of small size at birth on BMI trajectories is affected by ethnicity, maternal age, parity, pregnancy smoking, pregnancy diabetes, pregnancy hypertension, and prenatal and early life income adequacy and maternal education.

Objective 3:

To assess whether early life modifiable factors such as physical activity, sedentary screen time, and sleep duration have an effect on BMI at each time point and whether adjustment for these factors changes the magnitude of the effect of SGA status on BMI trajectories (see Figure 2.1).

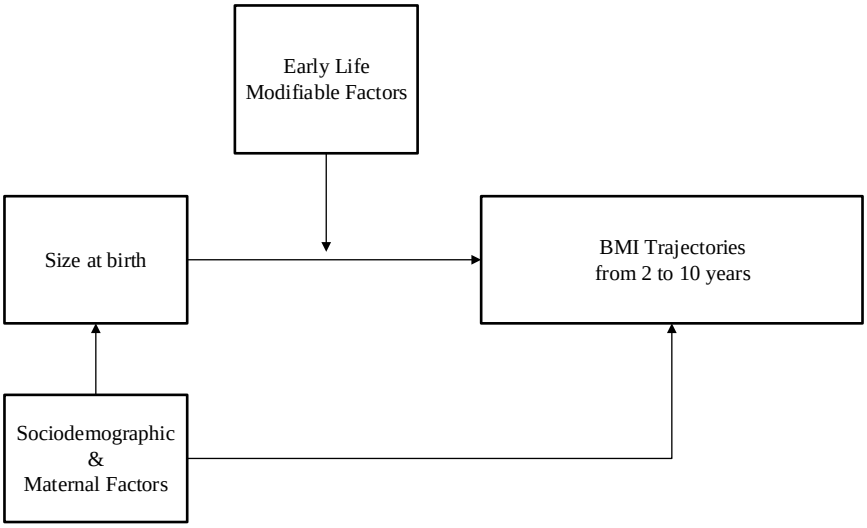


Figure 2.1 Conceptual model examining the effect of prenatal and early life sociodemographic and maternal variables, and also modifiable early life factors on BMI trajectories in growth restricted children.

2.2 Hypotheses

Objective 1:

It is hypothesized that children born SGA will have a greater rate of increase in BMI from ages 2 to 10 years than children born AGA. This reflects the suggestion of the fetal origins hypothesis that children born SGA are more susceptible to risk of obesity.

Objective 2:

It is hypothesized that adjustment for ethnicity, maternal age, parity, pregnancy smoking, pregnancy diabetes, pregnancy hypertension, and prenatal and early life income adequacy and maternal education, will diminish the association between SGA and childhood BMI trajectories. As discussed earlier, these sociodemographic and maternal factors have been shown to be associated with both small size at birth and obesity, and therefore are expected to confound the relationship between SGA and obesity.

Objective 3:

It is hypothesized that higher levels of physical activity and sleep duration will result in significantly lower BMI scores at each point in time. An increase in sedentary screen time is expected to result in significantly higher BMI scores at each point in time. Adjustment for physical activity, sedentary screen time, and sleep duration is also hypothesized to affect the magnitude of the effect of SGA status on childhood BMI trajectories, due to the explanatory power of these factors on the variance of these trajectories.

Chapter 3

3 Methods

This chapter begins with an overview of the survey used in this study (Section 3.1), followed by a description of the study population (Section 3.2). Subsequently, a description of the measures used in this study is provided (Section 3.3). This is followed by an overview of the modeling technique (latent growth curve modeling) in Section 3.4, and its considerations in Section 3.4.1. Finally, Section 3.5 explains how the statistical analyses were performed; Section 3.5.1 describes the preliminary analysis, and Sections 3.5.2 and 3.5.3 focuses on the estimation and evaluation of the unconditional and conditional models respectively.

3.1 Overview of Data Source

3.1.1 Survey

The National Longitudinal Survey of Children and Youth (NLSCY) is a long-term study conducted by Statistics Canada and Human Resources and Social Development Canada. The NLSCY followed a representative sample of Canadian children from birth to early adulthood, with data collection occurring at two-year intervals. The first collection of information (Cycle 1) took place in the winter and spring of 1994-1995 and the last collection took place in 2008-2009 (Cycle 8). The survey covered a wide range of topics regarding child growth and development. Additionally, information on the child's family members was also collected. The NLSCY identified one adult in the house as the person most knowledgeable (PMK) about the child. For children under 14 years, much of the information in the NLSCY was collected from the PMK, usually the mother by means of a household interview. At each cycle, the PMK provided information about the child's health, behaviour, education, and other characteristics.

3.1.2 Sampling Method

The NLSCY utilized the Labour Force Survey's (LFS) sampling frame to select participating households, the sampling unit of the survey. The LFS is a monthly household survey carried out by Statistics Canada and its sample is representative of the

civilian, non-institutionalized population, 15 years of age or older in the ten provinces. The LFS and thereby the NLSCY excluded residents of the three territories, those living on Indian Reserves, full-time members of the Canadian Armed Forces and inmates of institutions. At the time of the first NLSCY cycle, those excluded from the LFS survey represented approximately 2% of the Canadian population more than 15 years of age.

The NLSCY used a multi-stage cluster sampling approach to select households. In all sampled households, one person less than 11 years of age was selected at random to be a part of the longitudinal cohort. Please see the NLSCY User's Handbook and Microdata Guide for more information on the sampling design.[140]

Although the sampling frame of the LFS excluded the territories, collection for the territories was done separately in conjunction with the National Population Health Survey. The sample in the territories was selected from the population of private occupied dwellings. Institutions and unorganized areas were excluded for the Yukon sample. The Northwest Territories and Nunavut also excluded remote areas and very small communities. From each dwelling, up to three children were selected to be a part of the longitudinal cohort. The children from the territories were only followed until Cycle 4 of the NLSCY. At Cycle 4, data was not released for children from Nunavut.

To account for the complexity of the survey design (stratification, multiple stages of selection, and unequal probabilities of selection of respondents), survey weights were utilized so that the estimates would be free from bias.[141] Since BMI was first measured at Cycle 2 (when the respondents were 2 years of age), cross-sectional weights from this cycle were used so that the study population represents the Canadian population of 2 year olds as of 1996. For each case, the weight was calculated by dividing their cross-sectional weight by the average cross-sectional weight of the study population.

3.2 Study Population

The target population of this study were Canadian children between 2 to 10 years of age, who were born full-term SGA or AGA. Children were included in the study if they belonged to the longitudinal cohort of the survey and were two to three years of age by

Cycle 2 (the time of the first BMI measurement). Since there is no consensus in literature on how SGA status should be determined for children from multiple births, these children were excluded from the study. Pre-term (<37 weeks) and post-term (≥42 weeks) children were excluded from the sample since they are biologically different from those born at term, and as a result have different health outcomes in life. Large for gestational age (LGA) children (birth weight ≥ 90^{th} percentile for their gestational age and sex) were excluded from the population since they were not of interest to the study.

In this study, the children who met the inclusion and exclusion criteria were followed until Cycle 6 of the survey (approximately ten years from Cycle 1). By Cycle 6, all children in the sample were 10 years of age. Due to changes in measures of height and weight (from PMK report to self-report) at 12 years of age, the BMI trajectories of the cohort were not examined after Cycle 6.

Inherent to these conditions, the sample consisted of children who were <1 year at Cycle 1 (1994-1995), 2 years at Cycle 2 (1996-1997), 4 years at Cycle 3 (1998-1999), 6 years at Cycle 4 (2000-2001), 8 years at Cycle 5 (2002-2003), and 10 years at Cycle 6 (2004-2005).

3.3 Measures

3.3.1 Body Mass Index (outcome)

The primary outcome of this study was the body mass index (BMI) trajectories of the study population. Body mass index was used as the outcome measure, because direct measures of body fatness were not available in the NLSCY. Body mass index correlates well with body fatness and has been shown to be a valid measure of fatness in children.[142-147]

Using height and weight reports provided by the PMK, BMI values were calculated by dividing the weight in kilograms by the height in metres squared.

$$BMI = \frac{weight(kg)}{height\ (m)^2} \quad (3.1)$$

The calculated BMI scores were compared to the CDC growth charts from the year 2000 to identify biologically implausible values (independent of age and sex). To identify implausible values, BMI scores were converted to modified BMI Z-scores using CDC reference data.[148, 149] Any observation with a modified BMI Z-score <-4 or >+5 was flagged as implausible. The BMI Z-score cut-offs were based on CDC recommendations. Any values that were identified as implausible were then treated as missing values in the analyses. Body mass index values were calculated biennially for five time points, starting from 2 years of age (Cycle 2), until 10 years of age (Cycle 6). Body mass index was a continuous outcome in the analyses.

3.3.2 Size at Birth (primary predictor)

Before separating children into the two categories for size at birth, SGA or AGA, their percentile for birth weight for gestational age was calculated using data from PMK reports. First, birth weight was converted from kilograms to grams, and gestational age was converted from days to weeks. Small for gestational age children were then defined as those who had a birth weight below the 10th percentile for their sex and gestational age. Likewise, AGA children were defined as those who had a birth weight between the 10th and 90th percentiles (10th percentile $\leq$ AGA < 90th percentile). These cut-offs were used to create a binary indicator variable for size at birth (AGA = 0, SGA = 1).

The birth weight for gestational age percentile charts used to identify SGA and AGA children were created by Kramer et al. (2001) using all singleton births in Canada between 1994 and 1996 born between 22 and 43 weeks of gestation.[150] The reference population excluded children from multiple births, and infants born in Ontario due to concerns regarding the quality of birth weight and gestational age data from this province.[150]

3.3.3 Ethnicity

PMK were asked to report the child's racial background in Cycle 2 of the survey. Response categories were collapsed to create a binary indicator variable (white = 0,

visible minority = 1). Children who were identified by PMKs as belonging to more than one category were included in the visible minority group.

3.3.4 Maternal Age

Maternal age at the time of birth was reported in years at the first cycle. This variable was included as a continuous variable in the analyses.

3.3.5 Parity

In the first cycle of the survey, the NLSCY asked mothers "how many babies have you had?" Responses to this question were used to create a variable with two categories (primiparous or one past pregnancy = 0, multiparous or more than one past pregnancy = 1).

3.3.6 Pregnancy Smoking, Hypertension, and Diabetes

Similarly, in the first cycle, mothers were asked if they smoked, suffered from high blood pressure, and suffered from diabetes during their pregnancy with the child. Responses to each of these three questions were restricted to either 'yes' or 'no'. Based on these responses, three binary indicator variables were created to represent pregnancy smoking, hypertension and diabetes status (no = 0, yes = 1) in the analyses.

3.3.7 Maternal Education

For all six cycles considered in this study, the NLSCY asked PMKs about their highest completed level of education. The variable provided had 4 ordered categories: less than secondary, secondary school graduation, beyond high school, college or university degree (including trade). Those in the lowest category (less than secondary) were given a score of zero, and those in the highest category (college or university degree) had a score of three. Maternal education was included as a time-invariant and time-varying covariate in the analyses (see Section 3.5.3 and Appendix A for information on time-varying covariates). This variable was treated as a continuous variable rather than a categorical one in the analyses, because the relevant information regarding education was contained in the ranking number itself.

3.3.8 Income Adequacy

A variable based on household income and the number of people living in the household was provided in first five cycles of the NLSCY. This variable, referred to as income adequacy by the NLSCY, had five categories: lowest, lower middle, middle, upper middle, and highest. Those in the lowest income adequacy group were given a score of zero, and those in the highest income adequacy group were given a score of four.

Lowest income adequacy was defined as a household with an income less than $10,000 and 1 to 4 people; or a household with an income less $15,000 and 5 or more people.

Lower middle income adequacy was defined as a household with an income between $10,000 and $14,999 and 1 to 2 people; or households with an income between $10,000 and $19,999 and 3 to 4 people; or those with a household income between $15,000 to $29,999 and 5 or more people.

Middle income adequacy was defined as households with a total income between $15,000 and $29,999 and 1 to 2 people; or those households with an income between $20,000 and $39,999 and 3 to 4 people; or those with a household income between $30,000 and $59,999 and 5 or more people.

Upper middle income adequacy households were those with an income between $30,000 and $59,999 and 1 to 2 people; or a household with an income between $40,000 and $79,999 and 3 to 4 people; or a household with an income of $60,000 to $79,999 and 5 or more people.

Highest income adequacy households were those with an income greater than or equal to $60,000 with 1 to 2 people; or households with an income greater than or equal to $80,000 and 3 or more people.

Similar to maternal education, income adequacy was treated as a time-invariant and time-varying covariate. It was also utilized as a continuous variable rather than a categorical one in the analyses, because the relevant information regarding adequacy was contained in the ranking number itself.

3.3.9 Physical Activity

From Cycles 3 to 5, PMKs were asked three questions regarding their child's participation in physical activity. These questions asked how often in the past year outside of school hours, the child took lessons or instruction in organized physical activities with a coach or instructor (such as dance, gymnastics, or martial arts), organized physical activities with a coach or instructor (except dance, gymnastics, or martial arts), and unorganized physical activities without a coach or instructor. For all three questions, respondents had four options: almost never, about once a month, about once a week, a few times a week, and most days. Each category was given a score in accordance with its ranking. The lowest category, almost never, was given a score of zero, and the highest category, most days, was given a score of four. The responses to these questions were combined to create an additive physical activity score variable with values ranging from zero to twelve. The additive score was used to represent the physical activity level for each child and was included as a time-varying factor in the analyses.

3.3.10 Sedentary screen time

From Cycles 3 to 5, PMKs were asked how many hours a day on average their child spent watching television, videos or playing games. Sedentary screen time at each cycle was treated as a continuous, time-varying factor in the analyses. The survey also asked PMKs about the child's computer usage, but due to inconsistency in reporting across time, and missing data, computer usage was not included as a variable in the analyses.

3.3.11 Sleep duration

The survey also asked PMKs, from Cycles 4 to 6, how many hours a day on average their child slept. Like physical activity, and sedentary screen time, sleep duration was included as a continuous time-varying factor in the analyses.

3.4 Overview of Latent Growth Curve Modeling (LGCM)

Latent growth curve modeling (LGCM) is a statistical technique used to estimate growth curves or trajectories (change in an outcome over a period of time). Specifically, LGCM allows the following questions to be asked:

1. What is the mean initial level of the outcome of interest?
2. Does the mean level of the outcome change (increase or decrease) over time?
3. At what rate does the mean level change over time? Does it change in a linear or quadratic fashion?
4. Is there individual variability in the growth trajectory (variability in the initial level and rate of change)?
5. What factors account for the initial level and rate of change?

LGCM uses a structural equation modeling (SEM) framework to estimate growth trajectories. There are many benefits of using a SEM approach. First, LGCM has the ability to assess the fit of the model to the observed data using model fit indices. Second, unlike conventional procedures that assume there is no measurement error, LGCM adjusts for measurement error at each time point. Growth curve models also have more statistical power than traditional methods applied to the same data. Finally, the greatest benefit of using LGCM is its flexibility in handling complex models. Latent growth curve modeling can handle complexities such as partially missing data, uneven intervals between measurements, non-normally distributed outcome measures, complex non-linear trajectories, time-varying covariates, and multivariate growth processes.[151, 152] LGCM was carried out using MPlus 7 software.[141]

3.4.1 Model Considerations

3.4.1.1 Model Fit

Models were assessed for their fit to the observed data, by using sample size adjusted Bayesian Information Criterion (BIC) value comparisons. More information on the sample size adjusted BIC index can be found in Hancock and Samuelsen (2008).[153] Chi-square and related fit indices, such as the comparative fit index (CFI), Tucker-Lewis Index (TLI), and root mean square error of approximation (RMSEA) were not available due to the estimation of random intercepts and slopes.[141]

3.4.1.2 Time Scores

For each cycle of the survey, data were collected over a period of time between individuals. Consequently, the time difference between observations varied between individuals. Non-equidistant times of observation were adjusted for by using random factor loadings (time scores). In other words, time was an explanatory variable in the model. This was facilitated by the use of 'time scores' option in MPlus software. Factor loadings were calculated by subtracting the child's age at each cycle from their age at Cycle 2 (baseline).

3.4.1.3 Centering

The predictor variables included in each statistical model were centered. This was done so that the estimates of the intercept term would produce a meaningful value. In this study, the intercept term represents the average BMI at 2 years.

3.4.1.4 Missing Data

Missing data are an unavoidable part of longitudinal studies. One assumption that can be made about missing values is that they are missing completely at random (MCAR). The MCAR assumption can be defined as the probability that a missing value on a variable is unrelated to a person's score on any other variable. However, this assumption is unreasonable, because missing values in a dataset are usually related to other variables. In this study, an assumption was made that any missing data were missing at random (MAR). The MAR assumption states that a missing score on a variable does not depend on how the person actually would score on that variable, but that the missingness is related to other variables. There is no statistical test for the MAR assumption, since it is impossible to know if all of the appropriate variables that explain missingness have been included in the study. However, many key variables that may play a role in missingness, such as those relating to sociodemographics have been added to the analyses. A full-information maximum likelihood (FIML) approach has been shown to be valid for MAR data.[154] By default, MPlus uses FIML estimation to produce parameter estimates. FIML does not impute values for missing data, but uses all available information (variances and covariances) to produce a maximum likelihood estimation of parameters. Cases with

missing values for the outcome variable (BMI) were excluded only if the values were missing for all of the time points.

Missing data theory does not apply to observed covariates or exogenous variables (variables that do not receive a directional influence from other variables). Cases with missing values on such variables are excluded from the analyses because the model is estimated conditioned on them. This is a problem, since a missing value on any one of the observed covariates can result in exclusion of the case during model estimation. This may result in a significantly smaller sample size. To overcome this issue, some of these exogenous variables were converted to dependent or endogenous variables (variables that receive a directional influence from another variable) by specifying directional relationships between these observed covariates. A detailed justification of the conversion to endogenous variables can be found in Section 3.5.3 (Analysis for Model 3).

3.4.1.5 Power and Precision

Monte Carlo simulations have been recommended for calculating power and minimal sample size for such analyses.[155] However, it requires specification of a model with estimates of population values based on past studies. Since there are no past studies that have used a LGCM approach to this research topic, general sample size guidelines that have been suggested in literature was used. A minimum of 200 subjects per group (200 females and 200 males) have been recommended in literature as sufficient to provide enough power to conduct rigorous tests of data.[152, 156, 157] Some have suggested the use of 300 subjects per group for more stable estimates.[158]

3.5 Statistical Analyses

3.5.1 Preliminary Analysis

Weighted descriptive statistics were produced separately for males and females using survey weights provided by the NLSCY. Means and standard deviations were produced for all continuous variables (BMI, gestational age, additive physical activity score, sedentary screen time, and sleep duration). Likewise, for categorical variables (gender, size at birth, ethnicity, parity, pregnancy smoking, pregnancy hypertension, pregnancy

diabetes, maternal education, income adequacy, and physical activity participation), frequencies and percentages were produced.

3.5.2 Unconditional model (Model 1)

Prior to conducting any analyses on the effects of SGA on growth trajectories, an unconditional model (without predictor variables) was evaluated. The unconditional model estimates an underlying growth trajectory for each person across five time points (Cycles 2 to 6). The unconditional model estimates the intercept (initial BMI at 2 years), the mean rate of change of developmental trajectories, and the variability in the starting point and rate of change. The unconditional model and all subsequent models were estimated separately for females and males using survey weights from the NLSCY.

There was an a priori expectation that BMI trajectories have a quadratic trend since BMI usually shows a decline in infancy until four to six years of age, before showing a steady increase throughout childhood. Thus, in addition to a linear slope term, a quadratic term was added to the model to estimate the rate of change in the growth trajectories.

An age correction variable was added to the model to adjust for differences in age at the starting point of the trajectory. Since the expected age at the starting point of the trajectory (Cycle 2) was two years, the age correction variable was created by centering each child's age at Cycle 2 on two years. Growth trajectory parameters (intercept and linear slope terms) were then regressed on this variable to correct for age. To overcome computational issues related to model convergence, the variance of the quadratic slope term was fixed to zero. As a result, the quadratic slope term was not regressed on any covariates. A depiction of this model can be seen in Figure 3.1.

After model parameters were estimated, the fit of the model was assessed. If the model showed good fit to the observed data, means of the growth factors were evaluated to determine the average starting BMI at 2 years and growth trajectory. Subsequently, the variances for the intercept, and linear slope were checked to ensure that they were statistically significant ($p < 0.05$). Significant variances for the intercept and slope terms

implies variability in individual differences in growth over time and justifies further analyses.[159]

3.5.3 Conditional models (Models 2 to 4)

Analysis for Objective 1 (Model 2)

The first objective of the study was to assess whether the growth trajectories differ between SGA and AGA children. To answer this question, the unconditional model was extended to a conditional one by the inclusion of the main effect of SGA status. Specifically, the intercept and linear growth parameters were regressed on a variable for SGA status. This model is depicted in Figure 3.2.

Model parameters were evaluated in a similar manner to the unconditional model (Model 1). After assessing model fit, regression parameters for the SGA variable were evaluated since the main effect of SGA was of key interest. Next, similar to the unconditional model, variability in the intercept and linear slope terms were assessed for significance. Significant variances for these parameters justified carrying out the analysis for Objective 2. Changes in model estimates between models were also assessed; however, a formal statistical test was not carried out to determine if any changes were significant.

Analysis for Objective 2 (Model 3)

The second objective of the study was to assess if BMI trajectories differed between children born AGA and SGA after maternal and sociodemographic factors are taken into account. To answer this question, the previous model (Model 2) was expanded to include these factors.

In this model, the intercept term was regressed on the age correction variable and the time-invariant covariates (SGA status, maternal age ethnicity, parity, pregnancy diabetes, pregnancy smoking, and pregnancy hypertension, maternal education at Cycle 1, and income adequacy Cycle 1). The linear slope term was regressed on all of these variables, except maternal education and income adequacy at the time of the first cycle. Small for gestational age status was regressed on maternal age, ethnicity, parity, pregnancy

diabetes, pregnancy smoking, and pregnancy hypertension, and maternal education and income adequacy at the first cycle.

Income adequacy (from Cycles 2 to 5) and maternal education (from Cycles 2 to 6) also acted as time-varying covariates. The inclusion of time-varying covariates allowed for the estimation of the time-specific influence of the covariates on BMI at each time point, and the underlying growth trajectories after adjustment for these covariates. The relation between the growth trajectories and the time-varying covariates was modeled by regressing BMI scores on the time-varying covariate at the appropriate time. That is, BMI at Cycle 2 was regressed on maternal education at Cycle 2, BMI at Cycle 3 was regressed on maternal education at Cycle 2 and so on (see Figure 3.3). In this model and the subsequent model, the covariance between income adequacy at Cycle 5 and maternal education at Cycle 6 was fixed to zero to overcome computational issues and allow for model convergence.

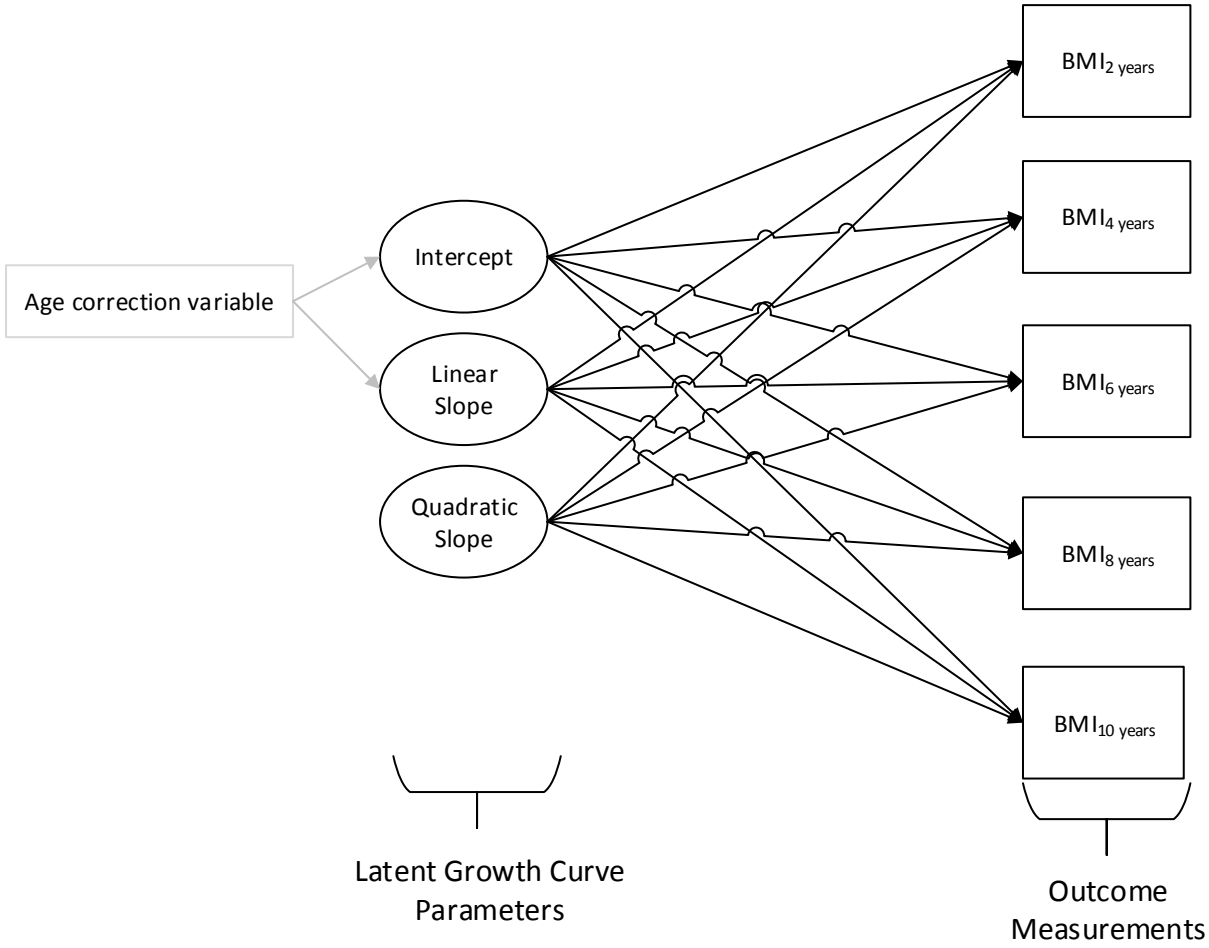
To avoid a large reduction in sample size due to missing data in exogenous variables, some predictors were converted from exogenous variables (variables that exert a directional influence) to endogenous variables (variables that receive a directional influence). This was accomplished by regressing parity, pregnancy diabetes, pregnancy smoking, and pregnancy hypertension, and maternal education and income adequacy at the first cycle on maternal age. These predictors were regressed on maternal age because it is a theoretically sound predictor of parity, pregnancy diabetes, pregnancy smoking, and pregnancy hypertension, maternal education, and income adequacy. Other directional relationships between predictor variables were not specified as they were not of interest to the study. Non-directional relationships (correlational associations) were specified between all of the predictors (see Figure 3.3).

This model was assessed in the same manner as the previous model (Model 2). However, in this model, the regression weights for SGA represent the effect of SGA on growth trajectories after adjustment for the other covariates.

Analysis for Objective 3 (Model 4)

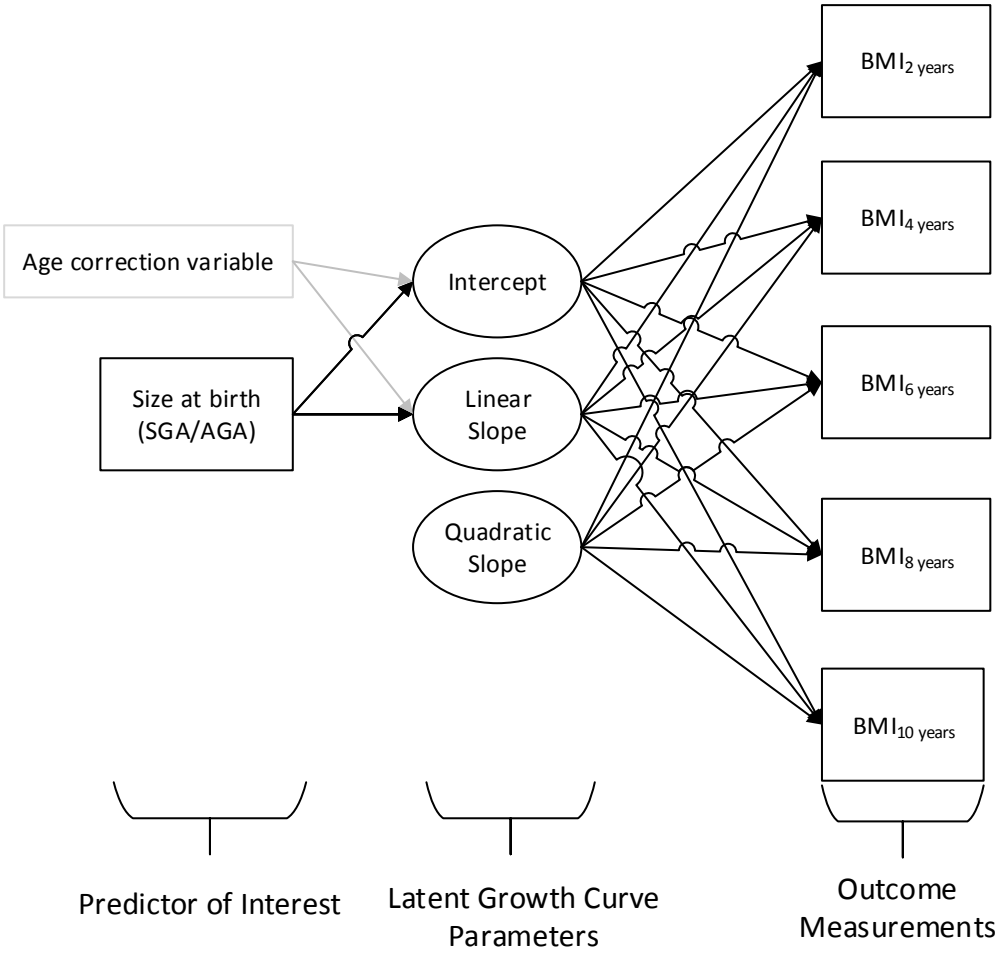
The final objective was to determine whether physical activity, sedentary screen time, and sleep duration had an effect on BMI at each time point and whether adjustment for these factors had an impact on the relationship between size at birth and BMI trajectories. To examine this objective, the previous model was extended to include these three time-varying factors. The additive physical activity score and sedentary screen time from Cycles 3 to 5, and sleep duration from Cycles 4 to 6 were taken into account in this model. Similar to the time-varying covariates of maternal education and income adequacy, BMI scores at each time point were regressed on the time-varying factors corresponding to the appropriate cycle. Non-directional associations (correlations) among these time-varying factors and other predictors were also specified.

Model estimates were interpreted in the same manner as Model 3. Now, the regression parameters are adjusted for the effect of these early life factors on BMI (see Figure 3.4).



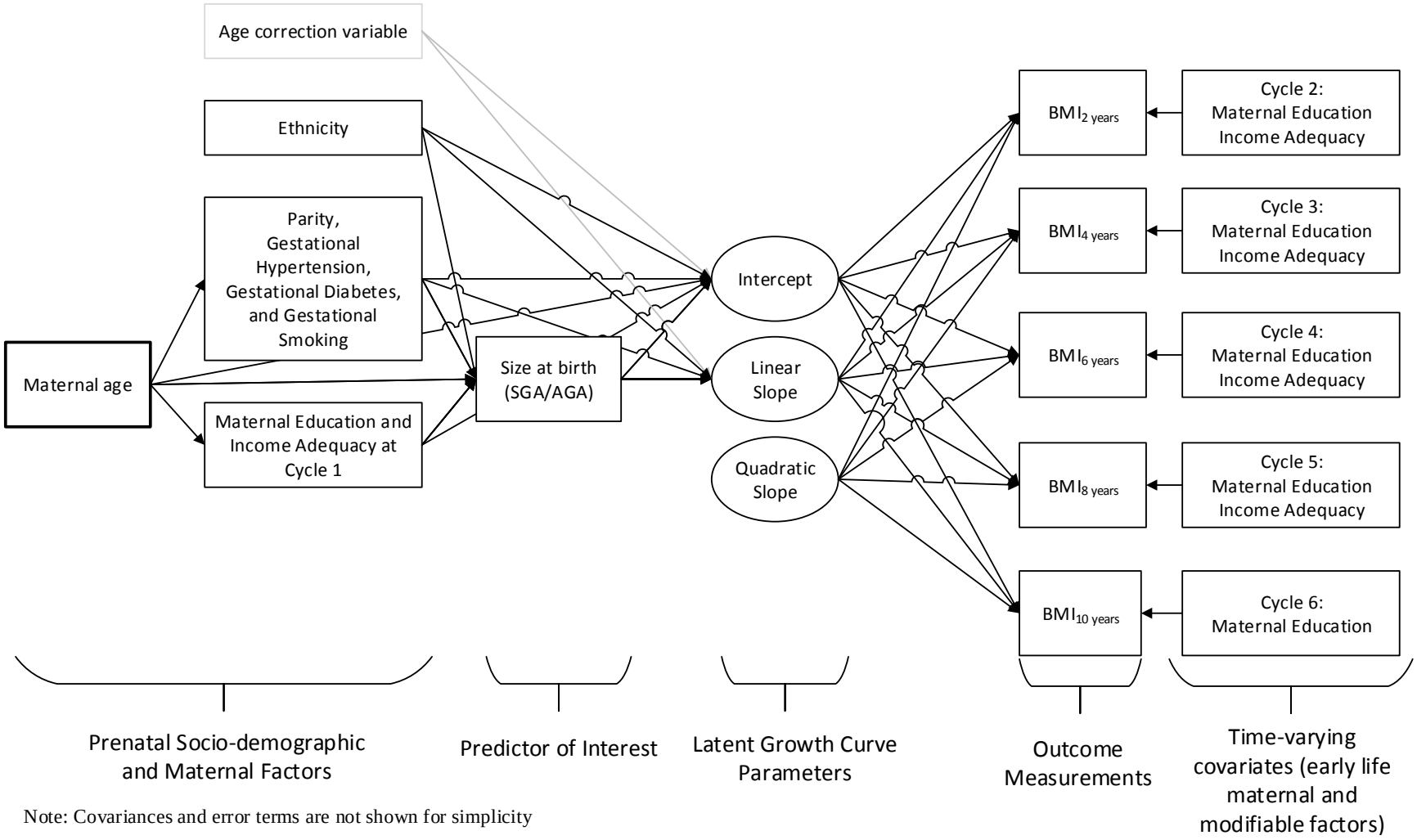
Note: Covariances and error terms are not shown for simplicity

Figure 3.1. Unconditional model (Model 1)



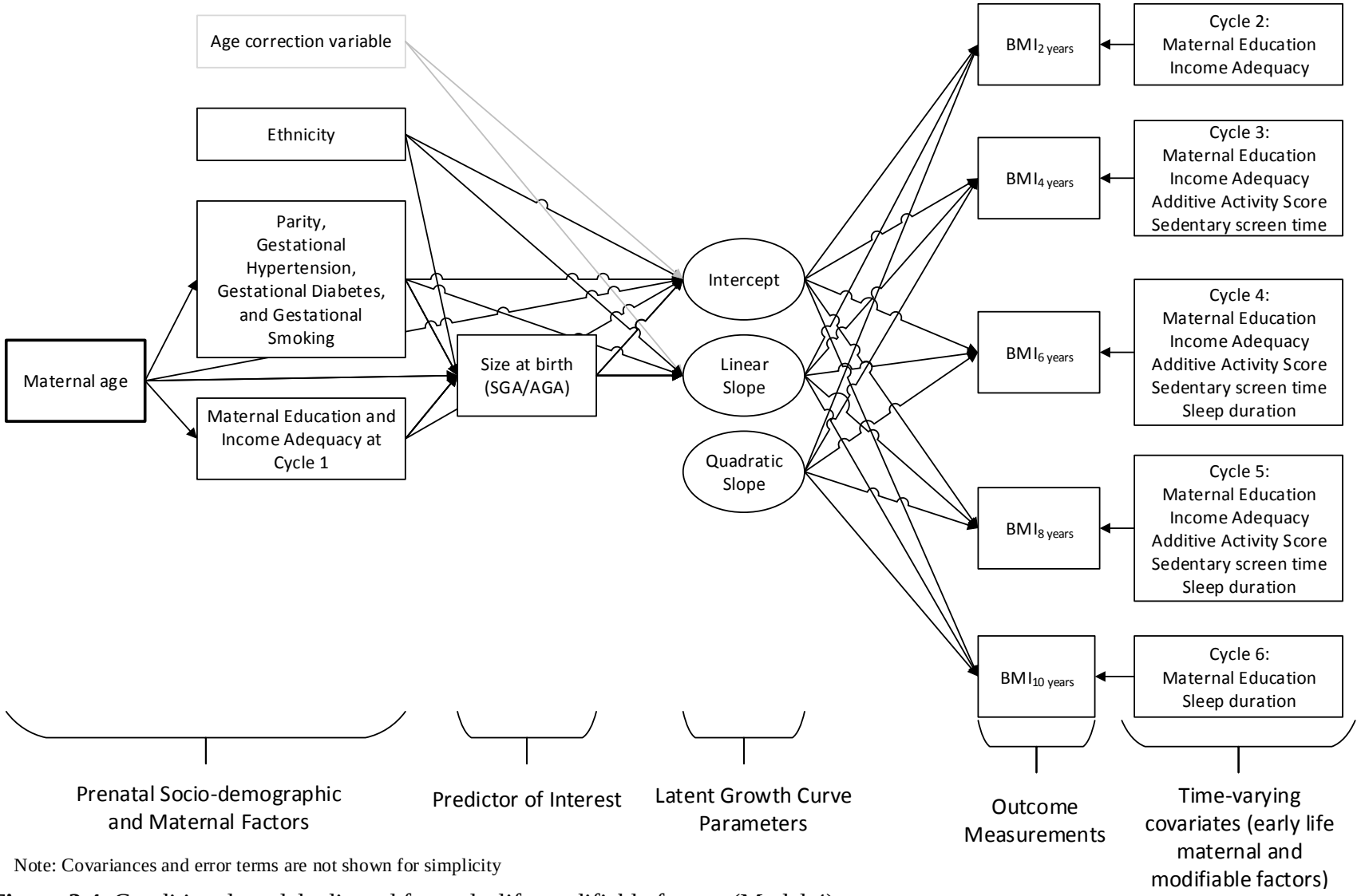
Note: Covariances and error terms are not shown for simplicity

Figure 3.2. Conditional unadjusted model (Model 2)



Note: Covariances and error terms are not shown for simplicity

Figure 3.3. Conditional model adjusted for prenatal and early life sociodemographic and maternal variables (Model 3)



Note: Covariances and error terms are not shown for simplicity

Figure 3.4. Conditional model adjusted for early-life modifiable factors (Model 4).

Chapter 4

4 Results

This chapter begins with a description of the study sample in Section 4.1 (including child and maternal characteristics in Sections 4.1.1 and 4.1.2). Section 4.2 describes the results from the latent growth curve analyses (Section 4.2), beginning with the results of the unconditional model (Section 4.2.1), followed by the conditional unadjusted model (Section 4.2.2), conditional model adjusted for maternal and sociodemographic factors (Section 4.2.3), and the conditional model adjusted for early life modifiable factors (Section 4.2.4).

4.1 Sample characteristics

The initial study sample, which included all children who were 2 to 3 years of age at the time of the first BMI measurement (Cycle 2), consisted of 1,782 children. After excluding children from multiple births, the sample was narrowed to 1,685 children. Exclusion of pre-term and post-term births further reduced the sample to 1,520 children. Finally, after excluding LGA children, the final sample size consisted of 1,273 children. In the cycles used in this study, PMKs were the biological mother for almost 90% of the children.

4.1.1 Child characteristics:

The sample consisted of 645 females (51%) and 628 males (49%). There was a greater proportion of females who were SGA than males. Approximately 12% of females (N=80) were SGA and 88% were AGA (N=565). In comparison, 8% of males were SGA (N=52) and 92% were AGA (N=575). Approximately 14% of females and 17% of males were visible minorities. The average age at each cycle was the same for males and females. Children in the study were on average 0.5 years at Cycle 1, 2.5 years at Cycle 2, 4.4 years at Cycle 3, 6.6 years at Cycle 4, 8.3 years at Cycle 5, and 10.6 years at Cycle 6. The mean BMI from Cycles 2 to 6 were also similar for males and females (see Table 4.1). In this

study, there were 129, 78, 21, 24, and 7 biologically implausible values for BMI at Cycles 2, 3, 4, 5, and 6 respectively. These values were treated as missing in the analyses.

The average gestational age was similar between males and females (approximately 39.37 weeks for females and 39.50 weeks for males). Around 14% (N=90) of females and 17% (N=106) of males were visible minorities (Table 4.1). On average, female AGA children were 0.51 metres at birth and 0.86 meters at Cycle 2. Likewise, male AGA children were 0.52 metres at birth and 0.89 metres at Cycle 2. In regards to those who were SGA, females were 0.48 metres at birth and 0.86 metres by Cycle 2. Male SGA children were 0.49 metres at birth and 0.88 metres by the second cycle (see Table 4.2). In regards to weight, female AGA children weighed 3.37 kg at birth and 13.94 kg by the second cycle. Male AGA children weighted 3.51 kg at birth and 14.58 kg at Cycle 2. Female SGA children were 2.63 kg at birth and 12.84 kg by Cycle 2. Similarly, male SGA children were 2.66 kg at birth and 14.41 kg by the second cycle (see Table 4.2).

Physical activity levels, represented by the additive score, increased from Cycles 3 to 5 in both genders. Females had a slightly higher activity level at Cycle 3, but males had greater levels by Cycles 4 and 5 (see Table 4.4). Sedentary screen time (TV use) was similar for males and females, and decreased over time. Females had approximately 2.3, 1.7, and 1.4 hours of sedentary screen time per day at Cycles 3, 4, and 5 respectively. Similarly, males had approximately 2.4, 1.8, and 1.4 hours of sedentary screen time per day at Cycles 3, 4, and 5 respectively (Table 4.4). The amount of sleep per day was similar for males and females, and decreased across time. Females on average got 10.1, 9.9, and 9.5 hours of sleep per day at Cycle 4, 5, and 6 respectively. Likewise, males got 10.3, 9.8, and 9.4 hours of sleep per day at Cycles 4, 5, and 6 respectively (Table 4.4).

4.1.2 Maternal characteristics

The mean maternal age at the time of the birth of the child was 29 years. For approximately 42% of mothers (N=490), the child in the survey was their first child. Around 10% of mothers (N=112) reported that they experienced high blood pressure during their pregnancy with the child. Also, 5% of mothers (N=53) said they suffered

from gestational diabetes. Additionally, about 25% of mothers (N=297) smoked during their pregnancy with the child (see Table 4.6).[†]

More than 40% of mothers had a college or university degree. By Cycle 6, this number rose to 52% of mothers. From Cycles 1 to 4, most mothers belonged to the upper middle category of income adequacy. At Cycle 5, most were in the highest category (see Table 4.7).

4.2 Statistical Analyses

LGCM automatically excluded cases from the analyses if they were missing for exogenous variables or in all observed variables. The sample size for these models were: 1,232 children for Models 1 and 2; 838 children for Model 3; 779 children for Model 4. A significance level of $\alpha = 0.05$ was used for all statistical tests.

4.2.1 Unconditional Model (Model 1)

The unconditional LGCM consisted of 635 females and 597 males (see Table 4.8). Model fit was assessed using sample size adjusted BIC values produced by MPlus (BIC = 21,470.94). The average BMI at 2 years (intercept) for females was 17.80 kg/m^2 ($p < 0.001$) and 17.65 kg/m^2 for males ($p < 0.001$). The linear slope term was -0.45 for females ($p = 0.001$) and -0.40 for males ($p < 0.001$). The estimate for the quadratic curvature term was 0.07 for both males and females ($p < 0.001$). The variance for the quadratic term was fixed to zero to allow model convergence in this model and all subsequent models. The intercept did not vary significantly with the linear slope term for either gender (females: est. = -0.20, $p = 0.305$; males: est. = -0.06, $p = 0.600$). There was significant variability in the intercept (females: est. = 1.93, $p = 0.028$; males: est. = 1.63, $p = 0.004$) and linear slope term (females: est. = 0.11, $p = 0.044$; males: est. = 0.11, $p = 0.003$).

[†] This estimate is lower than the national prevalence reported in 1994, and may be due to changes in smoking behaviour relating from pregnancy. The Survey of Smoking in Canada and the NPHS reported that approximately 35% of 25 to 44 year old Canadian women smoked at the beginning of 1994.[160]

4.2.2 Unadjusted Conditional Model (Model 2)

After adding the term for SGA status, the sample-size adjusted BIC value increased to 21,473.23. The number of cases remained the same as the unconditional model, at 653 females and 597 males (see Table 4.9).

The values of the intercept, linear slope, and quadratic term also stayed the same as the unconditional model. The covariance between the intercept and the linear term also remained statistically non-significant (females: est. = -0.20, p = 0.308; males: est. = -0.06, p = 0.566). The variability in the intercept and linear slope term remained significant. For the intercept, the variability decreased slightly in females and remained the same in males (females: 1.87, p = 0.029; males: 1.63, p = 0.004). The estimates for variability in the linear slope term remained the same as the unconditional model (females: est. = 0.11, p = 0.048; males: est. = 0.11, p = 0.003).

SGA status did not have a significant effect on the intercept (females: est. = -0.88, p = 0.129; males: est. = -0.02, p = 0.970) nor the linear growth term (females: est. = 0.06, p = 0.648; males: est. = -0.16, p = 0.127).

4.2.3 Model adjusted for prenatal and early life sociodemographic and maternal variables (Model 3)

The addition of maternal and sociodemographic variables reduced the total sample size of the model to 838 children (435 females and 403 males). The sample-size adjusted BIC value increased to 23,612.80 (see Table 4.10).

The estimate for the intercept decreased to 17.71 kg/m^2 in females ($p < 0.001$) and 17.47 kg/m^2 ($p < 0.001$) in males. The estimate for the linear term also decreased in females (est. = -0.52, $p < 0.001$), but remained the same in males (est. = -0.40, $p < 0.001$). The quadratic term, however, increased in females (est. = 0.08, $p < 0.001$) and remained unchanged for males (est. = 0.07, $p < 0.001$). The covariance between the intercept and the linear slope term remained statistically non-significant (females: est. = -0.14, p = 0.319; males: est. = -0.04, p = 0.713). The variability in the intercept term was no longer significant for females (est. = 1.11, p = 0.088) and males (est. = 1.00, p = 0.078),

indicating that these covariates sufficiently explain across child differences in the initial BMI. However, the variance of the linear term remained significant in both genders (females: est. = 0.10, p = 0.001; males: est. = 0.12, p < 0.001).

After accounting for other variables, the effect of SGA on the intercept was almost fully eliminated (est. = 0.003) in females. In males, the size of the effect decreased, and remained statistically non-significant (est. = -0.74; p = 0.382). Small for gestational age did not have an effect on the linear growth term for females (est. = -0.12, p = 0.482) and males (est. = -0.14, p = 0.351) after adjusting for these variables.

4.2.4 Model adjusted for early life modifiable factors (Model 4)

The final model included the time-varying effect of physical activity, sedentary screen time, and sleep duration. There were 779 children (408 females and 371 males) included in the analysis for this model. The sample-size adjusted BIC value increased to 26,675.27 (see Table 4.11).

The intercept estimate decreased slightly, but remained very similar to the previous model (females: est. = 17.67 kg/m^2, p < 0.001; males: est. = 17.44 kg/m^2, p < 0.001). The linear slope remained very similar. It decreased in females to -0.54 (p < 0.001) and increased in males to -0.38 (p < 0.001). The estimates for the quadratic slope term remained unchanged (females: est. = 0.08, p < 0.001; males: est. = 0.07, p < 0.001). The covariance between the intercept and linear slope term remained statistically non-significant (females: est. = -0.05, p = 0.712; males: est. = -0.05, p = 0.614). The variance of the intercept term also remained statistically non-significant for both females and males (females: est. = 0.64, p = 0.350; males: est. = 1.08, p = 0.051). The variance for linear term remained significant; it decreased slightly in females and stayed the same for males (females: est. = 0.09, p = 0.005; males: est. = 0.12, p < 0.001).

None of the early life factors (physical activity, sedentary screen, and sleep duration) had an effect on BMI at any time point. Additionally, SGA had no significant impact on the intercept and linear slope terms. The estimate of the effect of SGA on the intercept was -0.02 (p = 0.975) for females and -0.68 for males (p = 0.385). Likewise, the estimate for

the effect of SGA on the linear slope was -0.15 ($p = 0.394$) for females and -0.20 ($p = 0.184$) for males.

Table 4.1. Baseline child characteristics

	Females		Males	
	N	**%**	**N**	**%**
Gender	645	50.7	628	49.3
Size at Birth				
AGA	565	87.6	575	91.7
SGA	80	12.4	52	8.3
Ethnicity				
White	554	86.0	519	83.0
Visible Minority	90	14.0	106	17.0

	Females			Males		
	Mean	**N**	**S.D.**	**Mean**	**N**	**S.D.**
Gestational age - weeks	39.37	645	0.98	39.50	628	1.11
Age - months						
Cycle 1	6.27	645	3.21	6.31	628	3.28
Cycle 2	29.86	645	3.19	29.78	628	3.15
Cycle 3	52.60	603	3.47	52.33	572	3.19
Cycle 4	79.12	523	3.88	78.74	509	4.07
Cycle 5	99.49	518	3.46	99.23	491	3.66
Cycle 6	127.60	478	3.69	127.20	466	3.71
BMI - kg/m^2						
Cycle 2	17.85	486	2.90	17.62	478	2.50
Cycle 3	17.02	460	2.72	17.08	427	2.49
Cycle 4	17.04	400	3.30	17.18	376	3.42
Cycle 5	17.55	414	3.67	17.36	390	3.50
Cycle 6	18.44	413	3.65	18.74	409	4.06

Table 4.2. Catch-up growth from birth to two years

	Females						Males					
	AGA			SGA			AGA			SGA		
	Mean	**N**	**S.D.**	**Mean**	**N**	**S.D.**	**Mean**	**N**	**S.D.**	**Mean**	**N**	**S.D.**
Length at Birth (m)	0.51	522	0.03	0.48	72	0.03	0.52	548	0.03	0.49	39	0.03
Height at Cycle 2 (m)	0.86	500	0.10	0.86	75	0.09	0.89	510	0.09	0.88	50	0.10
Weight at Birth (kg)	3.37	565	0.32	2.63	80	0.21	3.51	575	0.33	2.66	52	0.26
Weight at Cycle 2 (kg)	13.94	537	2.00	12.84	76	2.10	14.58	548	1.98	14.41	48	2.39

Table 4.3. Early life characteristics - physical activity participation

	Females N (%)			Males N (%)		
	Cycle 3	**Cycle 4**	**Cycle 5**	**Cycle 3**	**Cycle 4**	**Cycle 5**
Organized physical activity (gymnastics or martial arts)						
Never	418 (72.2)	284 (55.5)	272 (52.7)	472 (85.1)	348 (71.9)	334 (69.0)
Once a month	6 (1.0)	13 (2.5)	11 (2.1)	13 (2.34)	9 (1.9)	7 (1.5)
Once a week	139 (24.0)	174 (34.0)	142 (27.5)	46 (8.3)	74 (15.3)	66 (13.6)
Few times a week or more	16 (2.8)	41 (8.0)	91 (17.6)	24 (4.3)	53 (11.0)	77 (15.9)
Organized physical activity (except gymnastics or martial arts)						
Never	387 (67.1)	250 (48.8)	193 (37.4)	382 (68.8)	187 (38.6)	131 (27.0)
Once a month	14 (2.4)	17 (3.3)	14 (2.7)	17 (3.1)	23 (4.8)	7 (1.4)
Once a week	148 (25.7)	140 (27.3)	172 (33.3)	121 (21.8)	147 (30.4)	121 (25.0)
Few times a week or more	28 (4.9)	105 (20.5)	137 (26.6)	35 (6.3)	127 (26.2)	226 (46.6)
Unorganized physical activity (without a coach)						
Never	230 (39.7)	184 (35.9)	119 (23.1)	234 (42.2)	124 (25.6)	88 (18.2)
Once a month	40 (6.9)	56 (10.9)	31 (6.0)	43 (7.7)	30 (6.2)	30 (6.2)
Once a week	82 (14.1)	68 (13.3)	93 (18.0)	55 (9.9)	85 (17.6)	66 (13.6)
Few times a week or more	228 (39.3)	204 (39.8)	273 (52.9)	222 (40.1)	245 (50.6)	300 (62.0)

Table 4.4. Early life characteristics – additive physical activity score, sedentary screen time, sleep duration

	Females			Males		
	Mean	**N**	**S.D.**	**Mean**	**N**	**S.D.**
Additive physical activity score (0 to 12)						
Cycle 3	3.00	578	2.45	2.67	555	2.30
Cycle 4	3.90	512	2.57	4.33	484	2.49
Cycle 5	4.90	516	2.60	5.24	484	2.58
TV Use - hours						
Cycle 3	2.34	569	1.24	2.35	548	1.35
Cycle 4	1.65	512	0.79	1.79	489	1.11
Cycle 5	1.43	516	0.84	1.44	483	0.85
Sleep - hours						
Cycle 4	10.13	510	1.04	10.26	484	0.98
Cycle 5	9.87	516	0.97	9.75	485	1.02
Cycle 6	9.53	475	0.91	9.44	465	0.91

Table 4.5. Correlation between early life modifiable factors and BMI scores

	Females	**Males**
	r	*r*
BMI at Cycle 3 and Physical Activity at Cycle 3:	-0.13	-0.03
BMI at Cycle 4 and Physical Activity at Cycle 4:	-0.04	-0.07
BMI at Cycle 5 and Physical Activity at Cycle 5:	0.01	-0.16
BMI at Cycle 3 and TV Use at Cycle 3:	-0.01	-0.07
BMI at Cycle 4 and TV Use at Cycle 4:	0.12	0.00
BMI at Cycle 5 and TV Use at Cycle 5:	0.00	0.03
BMI at Cycle 4 and Sleep at Cycle 4:	-0.10	0.02
BMI at Cycle 5 and Sleep at Cycle 5:	-0.11	-0.03
BMI at Cycle 6 and Sleep at Cycle 6:	-0.05	0.07

Table 4.6. Maternal characteristics - health

	Mean	**N**	**S.D.**
Maternal age – years	29	1267	5
	N	**%**	
Parity			
Primiparous	490	42.1	
Multiparous	673	57.9	
Pregnancy high blood pressure			
No	1052	90.4	
Yes	112	9.6	
Pregnancy diabetes			
No	1110	95.4	
Yes	53	4.6	
Pregnancy Smoking			
No	868	74.5	
Yes	297	25.5	

Table 4.7. Maternal characteristics – education and income adequacy

	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Maternal Education – N (%)						
Less than secondary	214 (16.8)	158 (12.4)	124 (10.6)	100 (9.8)	133 (13.3)	124 (13.3)
Secondary school graduation	213 (16.8)	210 (16.5)	181 (15.4)	217 (21.3)	210 (21.1)	213 (22.8)
Beyond high school	320 (25.2)	333 (26.2)	295 (25.1)	222 (21.8)	161 (16.2)	112 (12.0)
College or university degree (including trade)	524 (41.2)	571 (44.9)	575 (48.9)	480 (47.1)	493 (49.5)	486 (52.0)
Income Adequacy – N (%)						
Lowest or Lower middle	237 (18.6)	241 (18.9)	168 (14.3)	78 (7.6)	73 (7.2)	-
Middle	390 (30.6)	403 (31.7)	354 (30.1)	298 (28.9)	197 (19.5)	-
Upper middle	478 (37.6)	449 (35.3)	391 (33.3)	351 (34.0)	348 (34.5)	-
Highest	168 (13.2)	180 (14.1)	263 (22.4)	305 (29.6)	390 (38.7)	-

Table 4.8. Unconditional unadjusted model (Model #1)

Model fit measures								
Loglikelihood (Null value):	-10,684.25		Total observations:	1,232				
Loglikelihood Scaling factor:	2.99		Free parameters:	26				
Sample-Size Adjusted BIC:	21,470.94							
	Females (N=635)				**Males (N=597)**			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Means								
α (intercept)	17.80	0.22	79.29	0.000	17.65	0.15	116.50	0.000
β_1 (linear term)	-0.45	0.14	-3.33	0.001	-0.40	0.10	-3.87	0.000
β_2 (quadratic term)	0.07	0.02	4.26	0.000	0.07	0.01	5.21	0.000
Covariances								
α with β_1	-0.20	0.20	-1.03	0.305	-0.06	0.11	-0.53	0.600
Variances								
α (intercept)	1.93	0.88	2.20	0.028	1.63	0.56	2.89	0.004
β_1 (linear term)	0.11	0.05	2.01	0.044	0.11	0.04	2.99	0.003
β_2 (quadratic term)	Not estimated (variance fixed to zero)							

Table 4.9. Conditional model adjusted for SGA status (Model #2)

Model fit measures								
Loglikelihood (Null value):	-10,677.52		Total observations:	1,232				
Loglikelihood Scaling factor:	2.87		Free parameters:	30				
Sample-Size Adjusted BIC:	21,473.23							
	Females (N=635)				**Males (N=597)**			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Means								
α (intercept)	17.80	0.22	81.37	0.000	17.65	0.15	116.51	0.000
β_1 (linear term)	-0.45	0.14	-3.36	0.001	-0.40	0.10	-3.87	0.000
β_2 (quadratic term)	0.07	0.02	4.27	0.000	0.07	0.01	5.19	0.000
Covariances								
α with β_1	-0.20	0.19	-1.02	0.308	-0.06	0.11	-0.57	0.566
Variances								
α (intercept)	1.87	0.85	2.19	0.029	1.63	0.56	2.90	0.004
β_1 (linear term)	0.11	0.05	1.98	0.048				
β_2 (quadratic term)	Not estimated (variance fixed to zero)							
Regression Coefficients								
α on SGA	-0.88	0.58	-1.52	0.129	-0.02	0.57	-0.04	0.970
β_1 on SGA	0.06	0.14	0.46	0.648	-0.16	0.11	-1.53	0.127

Table 4.10. Conditional model adjusted for maternal and sociodemographic factors (Model #3)

Model fit measures								
Loglikelihood (Null value):	-11,571.70		Total observations:	838				
Loglikelihood Scaling factor:	2.62		Free parameters:	132				
Sample-Size Adjusted BIC:	23,612.80							
	Females (N=435)				**Males (N=403)**			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Means	17.71	0.22	79.16	0.000	17.47	0.18	97.48	0.000
α (intercept)	-0.52	0.13	-3.97	0.000	-0.40	0.11	-3.65	0.000
β_1 (linear term)	0.08	0.02	5.10	0.000	0.07	0.01	5.10	0.000
β_2 (quadratic term)								
Covariances								
α with β_1	-0.14	0.14	-1.00	0.319	-0.04	0.10	-0.37	0.713
Variances								
α (intercept)	1.11	0.65	1.71	0.088	1.00	0.57	1.76	0.078
β_1 (linear term)	0.10	0.03	3.31	0.001	0.12	0.03	4.01	0.000
β_2 (quadratic term)	Not estimated (variance fixed to zero)							
Regression Coefficients								
α on SGA	0.00	0.66	0.00	0.997	-0.74	0.85	-0.88	0.382
β_1 on SGA	-0.12	0.17	-0.70	0.482	-0.14	0.15	-0.93	0.351

Table 4.11. Conditional model adjusted for maternal, sociodemographic, and early life modifiable factors (Model #4)

Model fit measures								
Loglikelihood (Null value):	-13,062.50		Total observations:	779				
Loglikelihood Scaling factor:	2.54		Free parameters:	158				
Sample-Size Adjusted BIC:	26,675.27							
	Females (N=408)				**Males (N=371)**			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Means								
α (intercept)	17.67	0.23	76.67	0.000	17.44	0.18	97.25	0.000
β1 (linear term)	-0.54	0.14	-3.89	0.000	-0.38	0.11	-3.39	0.001
β2 (quadratic term)	0.08	0.02	4.88	0.000	0.07	0.01	4.84	0.000
Covariances								
α with β_1	-0.05	0.14	-0.37	0.712	-0.05	0.10	-0.51	0.614
Variances								
α (intercept)	0.64	0.69	0.93	0.350	1.08	0.55	1.95	0.051
β1 (linear term)	0.09	0.03	2.81	0.005	0.12	0.03	4.23	0.000
β2 (quadratic term)	Not estimated (variance fixed to zero)							
Regression Coefficients								
α on SGA	-0.02	0.69	-0.03	0.975	-0.68	0.78	-0.87	0.385
β1 on SGA	-0.15	0.17	-0.85	0.394	-0.20	0.15	-1.33	0.184

Chapter 5

5 Discussion

This chapter begins with an overview of the findings of this study (Section 5.1), followed by an interpretation of the main findings (Section 5.2). Then, a review of the limitations of this study is provided (Section 5.3), followed by its strengths (Section 5.4). The subsequent section provides a conclusion of the overall findings and recommendations for future research (Section 5.5).

5.1 Overview of study findings

BMI trajectories

In this study, BMI trajectories were modeled from 2 to 10 years for a sample of SGA and AGA singletons born at term. The results showed that BMI trajectories for males and females increased over time in a quadratic fashion. This was confirmed by the significant estimate for the quadratic term in the unconditional model. As expected, BMI declined in infancy until sometime between 5 to 6 years, and then increased over time. On average, males had a lower BMI from 2 to 5 years, but had a higher BMI from about 5 to 10 years of age. As indicated by the statistically non-significant covariance between the intercept and linear slope terms, BMI at 2 years did not affect the rate of change in BMI over time. That is, whether a child had a low or high BMI at 2 years, did not affect how rapidly his/her BMI changed over time. In the unconditional, unadjusted model, the unexplained variance in the intercept and linear slope terms were significant. This indicated that more variables could be added to model to explain across child differences in growth trajectories.

SGA status and BMI trajectories

SGA status did not have an effect on BMI trajectories of children in the unadjusted model. The addition of the SGA term did not have a great impact on the variance estimates. The variance in the intercept decreased by 3% for females, and remained unchanged in males, while the variance in the linear term was unaffected.

Adjustment for maternal and sociodemographic factors

After adjusting for maternal and sociodemographic factors (ethnicity, maternal age, parity, gestational hypertension, gestational diabetes, gestational smoking, maternal education, and income adequacy), SGA status still had no effect on the BMI growth trajectories of children. After taking these factors into account the variance of the intercept was no longer significant, suggesting that these factors sufficiently explain the individual variability in the starting BMI at 2 years. Interestingly, the variance in the linear term decreased by 10% in females and increased by 10% in males. This indicates that, the BMI trajectory for females is better representative of the females in the study population than the trajectory for males is representative of the males in the study population.

Adjustment for early life modifiable factors

Taking into account early life factors such as physical activity, sedentary screen time, and sleep duration, did not affect the growth trajectories to a great degree. The estimate for the intercept decreased by less than 1% for females and males, while the estimates for the linear slope decreased by 4% in females and increased by 5% in males. The estimate for quadratic growth term showed no change. The addition of these early life factors, however, explained 25% of the variance of the linear growth term in females. There was no change in the variance of the linear term for males. This suggests that these factors better accounted for the differences in growth trajectories for females than males.

More importantly, in this fully adjusted model, SGA status still had no effect on the growth trajectory parameters. Estimates of the regression coefficients that represent the effect of SGA on the growth trajectory only showed marginal change and remained not statistically significant. Also, the levels of physical activity, sedentary screen time, and sleep duration had no effect on the BMI score at each time point.

5.2 Interpretation of findings

5.2.1 BMI Trajectories

A surprising finding of this study was that average BMI trajectory for the study cohort was similar to that of children at higher risk for overweight and obesity. When compared to the WHO growth charts for Canada, which depict optimal growth, the BMI of the study population from 2 to 10 years, closely followed those in the 85th percentile of BMI-for-age.[161] Comparisons to CDC growth charts also show that the study population's BMI trajectory was similar to those in between the 75th and 85th percentiles of BMI.[162] Studies have shown that being above the 85th percentile for BMI is associated with greater risk of obesity and other chronic diseases later in life.[15, 163] This highlights the significance of the childhood obesity problem in Canada and the importance of examining the mechanisms of childhood obesity. In addition to the increasing BMI epidemic, a factor that can account for this phenomenon is error in anthropometric reports, which may have led to overestimation of BMI scores (further discussed in Section 5.3.1).

5.2.2 SGA status and BMI growth trajectories

The fetal origins hypothesis postulates the relationship between events during fetal growth and later health. Adaptations in response to insults during fetal growth are believed to contribute to the development of chronic diseases later on in life. At birth, evidence of a poor intrauterine environment affecting fetal growth (or fetal growth restriction) is evidenced by the surrogate measure of size at birth or birth weight for gestational age. The findings of this study do not lend support to the hypothesis that being born SGA at term has an impact on the BMI trajectories of children. Even after adjusting for maternal, sociodemographic, and early life variables, the association between SGA and weight status later in life was not statistically significant. Similar results have been found in other studies that examined the relationship between SGA and later weight status.[47, 164, 165] However, of the three studies that reported a similar finding to this study, two included pre-term children in the study population.[47, 164] Nonetheless, experimental animal studies have found that insults in utero lead to lifelong alterations in metabolism, physiology, and pathology.[15] There is also robust epidemiological evidence that small

size at birth is associated with chronic diseases such as hypertension, glucose intolerance, type 2 diabetes, and coronary heart disease incidence and mortality.

5.2.3 Early life modifiable factors

Some investigators have suggested that catch-up growth in growth restricted children plays a role in later obesity risk. In the current study, children who were born SGA experienced growth between birth and two years such that by two years they had a similar average weight and BMI as AGA children (see Table 4.2). By two years, female AGA children had an average weight of 13.94 ± 2.00 kg, while SGA children had a weight of 12.84 ± 2.10 kg. Similarly, male AGA children had a weight of 14.58 ± 1.98 kg at two years, while SGA males had a weight of 14.41 ± 2.31 kg. Also, the growth trajectories of SGA children were no different than those of AGA children after two years. This would indicate that catch-up growth in SGA children did not lead to a growth trajectory associated with greater risk of disease.

Physical activity and sedentary screen time from 4 to 8 years, and sleep duration from 6 to 10 years had no impact on the growth trajectories of children. They were also weakly correlated with BMI (Table 4.5) and not significant predictors of BMI at any point in time. This was a surprising finding, because these factors relate to energy expenditure and have been identified in literature as factors that mitigate the risk of weight related diseases.[135, 166-169] A possible reason for the statistically non-significant findings is that these early life factors may not have been representative of their true levels in these factors since they were based on PMK reports. A lack of availability of direct measures may have led to underestimation of the level of physical activity and sedentary screen time. In fact, the highest average additive physical activity score (which can range from zero to twelve) was only five (at Cycle 5) for females and males (see Table 4.4). Additionally, only television viewing was used to define sedentary screen time. Other measures of sedentary screen time such as computer usage were excluded due to poor data quality (high levels of missing data and lack of consistency in questioning between cycles). Furthermore, information on diet was not available in the survey and was not accounted for in this study. Consequently, not taking into consideration such factors

related to energy intake and expenditure may have confounded the relationship between physical activity, sedentary screen time (television viewing), sleep duration and BMI.

5.3 Limitations

5.3.1 PMK Reports

Since birth weight and gestational age information were based on PMK reports, recall bias may have affected the accuracy of this information. Also, PMK reports on child height and weight may have affected BMI scores. For children less than 12 years of age, parental report is expected to overestimate BMI scores since parents tend to underestimate their children's height.[170, 171] Assuming inaccuracies in anthropometric reports were relatively consistent throughout study, they are expected to have a minimal influence on the interpretation of study findings, since the focus of this study was on the shape of the trajectories. A lack of more direct measures of physical activity, sedentary screen time, and sleep duration may have also affected the accuracy of these measures.

5.3.2 Measures

Adiposity

A limitation of this study was that BMI was the only measure of adiposity available. Though it is a valid measure of total body fatness, BMI does not detect differences in fat distribution within a body. When SGA individuals become obese, they tend to accumulate more central fat. Increased central fat is a risk factor for diabetes mellitus and cardiovascular diseases.[172] Thus it may be possible for SGA children to have a similar BMI to AGA children while also having greater central obesity. If SGA children indeed had greater central fatness, this would give support to the fetal origins of obesity hypothesis.[164, 172]

Diet

Rising levels of childhood obesity can be partly attributed to a shift in dietary patterns towards increased intake of energy dense foods. This study was not able to include information on dietary intake, because such information was not available in the NLSCY.

As a result, it may be possible that the statistically non-significant effect of SGA on the parameters for BMI trajectories were a result of not taking into account the dietary patterns of the children in the study.[173] Though, there are no reports to date that suggest that SGA children have dietary patterns that differ from AGA children.

5.3.3 Attrition

Statistically non-significant effects of SGA on childhood BMI trajectories may also be due to attrition. Indeed, as cycles progressed there was greater attrition. This results in model estimates of the trajectory being based on fewer cases over time. This may have influenced the statistical power such that it was difficult to detect significant effects.

5.4 Strengths

5.4.1 Sampling design

The sampling design used by the NLSCY resulted in an initial study sample that is nationally representative. As a result, a strength of this study is its generalizability to the Canadian population of AGA and SGA singletons born at term who were 2-3 years as of 1996.

5.4.2 Use of SGA

One of the strengths of the study was the use of SGA (<10^{th} percentile of birth weight for gestational age and sex) as a measure of growth restriction rather than low birth weight (<2,500 grams). Compared to low birth weight as a measure of growth restriction, SGA captures more growth restricted infants.[62] In fact, most growth restricted infants, have a birth weight that is higher than the cut-off for low birth weight.[90]

5.4.3 Growth curve modeling

This study was one of the first to use growth curve modeling to analyze the relationship between SGA and later growth. Compared to analytic techniques that simply look at predictors of weight status at one point in time, the modeling of BMI over time has many advantages. By utilizing LGCM techniques, much more can be understood about the pattern of growth. Latent growth curve modeling allows for the specification of more

complex models when evaluating a causal hypothesis. It can also take into account the timing of the effect of predictors and their change over time. LGCM also adjust for errors in measurement that might exist in predictors and outcomes.[158] Unlike some analytic methods, which assume that the intercept and slope are independent, LGCM assumes a covariance term.[174]

Additionally, LGCM utilizes a full information maximum likelihood (FIML) approach to produce model estimates. Using a FIML approach minimizes the bias in model parameter estimates and standard errors because it uses all available information.[175] Traditional methods such as listwise deletion often result in a large number of cases being dropped from the sample. It also assumes that the data are missing completely at random (MCAR). The MCAR assumption does not hold true in most studies. Similarly, with mean substitution, the mean value may be a poor estimate when the missing data are not like the non-missing data. Mean substitution also reduces the variance since cases are assigned the same value. Also, the assigned value may not be a reasonable one.[175]

5.4.4 Life course approach

The life course approach studies the effects of biological and social exposures through the lifespan on chronic disease risk. This study recognized the importance of such an approach and incorporated physical and social exposures of health for a more comprehensive view of disease risk. The life course approach also takes into account the timing of exposure variables and how these exposure variables relate to the outcome. The analytic technique used in this study allowed for the timing and change in levels to be taken into account. Particularly, it was possible to incorporate the change in measures such as maternal education, income adequacy, physical activity, sedentary screen time and sleep duration through childhood into the analyses.

5.5 Conclusions and Recommendations

In order to examine the fetal origins of obesity hypothesis, this study looked at the growth trajectories in children born SGA or AGA at term. The results showed that SGA children did not have a different growth trajectory compared to AGA children born at term after adjusting for many factors. To date, only a few studies of sufficient methodological

quality have been published that have found similar results. This study did find that on average, BMI of the study population were indicative of those at high risk of overweight and obesity. Future studies should attempt to incorporate direct measures of obesity and central adiposity as well as measures such as diet. With the prevalence of obesity on the rise, it is becoming more important than ever to study not only the risk factors, but also those factors that decrease the risk of disease in children. To tackle the issue of obesity, it is recommended that investigators use a life course perspective with an analytic technique similar to the one used in this study. Doing so will allow for a more contextual and comprehensive understanding of this complex and multifactorial disease. This study is one of the first to utilize such an approach and provides a framework for future research relating to the fetal origins hypothesis, childhood obesity, and other chronic disease.

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Appendix A: Latent Growth Curve Model Equations

Unconditional Model (Model 1):

The unconditional model can be represented by the equation:

$$BMI_{it} = \alpha_i + \beta_{1_i}\lambda_t + \beta_{2_i}\lambda_t^2 + \epsilon_{it} \quad \text{(A.1)}$$

BMI_{it} is the value for BMI for the *i*th child at time *t*, α_i is the intercept of the growth trajectory for the *i*th child (initial BMI at 2 years of age), β_{1_i} is the linear slope for the *i*th child, β_{2_i} is the quadratic slope term representing the curvature of the growth trajectory for the *i*th child, λ_t is the factor loading (time score) representing the value of time at time point *t*, and ϵ_{it} is the random error for the *i*th person at time *t*. Due to individually varying times of observations, the value of the factor loading, λ_t, varies among individuals. When the times of observation are the same among individuals, time scores can characterized by the values 0, 1, 2, 3, and 4 for *t* = 0, 2, 4, 6, and 8 respectively. The time point, *t* = 0 corresponds to the first BMI measurement and *t* = 8 corresponds to the last measurement. In this study, however, since each child has a different time of measurement, each child has a different factor loading at time point, *t*. Factor loadings were calculated by subtracting the child's age at each cycle from their age at Cycle 2 (baseline).

The intercept, linear slope, and quadratic slope terms can be represented as follows:

$$\alpha_i = \mu_\alpha + \gamma_{\alpha_{centredage}} x_{centredage_i} + \zeta_{\alpha_i} \quad \text{(A.2)}$$

$$\beta_{1_i} = \mu_{\beta_1} + \gamma_{\beta_{1_{centredage}}} x_{centredage_i} + \zeta_{\beta_{1i}} \quad \text{(A.3)}$$

$$\beta_{2_i} = \mu_{\beta_2} \quad \text{(A.4)}$$

The term μ_α, is the mean intercept, μ_{β_1} is the mean linear slope, and μ_{β_2} is the mean quadratic curvature across all cases, and ζ_{α_i}, $\zeta_{\beta_{1_i}}$, and $\zeta_{\beta_{2_i}}$represent the random error (individual deviations from their respective means). To overcome computational issues

related to model convergence, the variance of the quadratic slope term, $\zeta_{\beta_{2_i}}$, was fixed to zero. As a result, the quadratic slope term was not regressed on any covariates. The terms $\gamma_{\alpha_{centredage}}$ and $\gamma_{\beta_{1_{centredage}}}$ represent regression coefficients that describe the linear relationship between the age correction variable, $x_{centredage_i}$, and the intercept and linear slope equations (see Figure 3.1).

Conditional Model with SGA term (Model 2):

The conditional model departs from the unconditional model in the equations for the intercept and linear slope:

$$\alpha_i = \mu_\alpha + \gamma_{\alpha_{centredage}} x_{centredage_i} + \gamma_{\alpha_{SGA}} x_{SGA_i} + \zeta_{\alpha_i} \quad \text{(A.5)}$$

$$\beta_{1_i} = \mu_{\beta_1} + \gamma_{\beta_{1_{centredage}}} x_{centredage_i} + \gamma_{\beta_{1_{SGA}}} x_{SGA_i} + \zeta_{\beta_{1i}} \quad \text{(A.6)}$$

These equations now include the regression coefficients, $\gamma_{\alpha_{SGA}}$ and $\gamma_{\beta_{1_{SGA}}}$, which relate SGA status (x_{SGA_i}) to the intercept and linear slope. The equations for BMI_{it} and β_{2_i} remained unchanged (see Equation A.1, Equation A.4, and Figure 3.2).

Conditional Model Adjusted for Prenatal and Early Life Sociodemographic and Maternal Variables (Model 3):

This model can be summarized by following equations:

$$BMI_{it} = \alpha_i + \beta_{1_i}\lambda_t + \beta_{2_i}\lambda_t^2 + \gamma_{matedu_{t_{cycles2to6}}} x_{matedu_{it_{cycles2to6}}} + \gamma_{income_{t_{cycles2to5}}} x_{income_{it_{cycles2to5}}} + \epsilon_{it} \quad \text{(A.7)}$$

$$\alpha_i = \mu_\alpha + \gamma_{\alpha_{centredage}} x_{centredage_i} + \gamma_{\alpha_{SGA}} x_{SGA_i} + \gamma_{\alpha_{ethnicity}} x_{ethnicity_i} + \gamma_{\alpha_{parity}} x_{parity_i} + \gamma_{\alpha_{BP}} x_{BP_i} + \gamma_{\alpha_{diabetes}} x_{diabetes_i} + \gamma_{\alpha_{smoking}} x_{smoking_i} + \gamma_{\alpha_{matedu@cycle1}} x_{matedu@cycle1_i} + \gamma_{\alpha_{income@cycle1}} x_{income@cycle1_i} + \gamma_{\alpha_{maternalage}} x_{maternalage_i} + \zeta_{\alpha_i} \quad \text{(A.8)}$$

$$\beta_{1_i} = \mu_{\beta_1} + \gamma_{\beta_{1_{centredage}}} x_{centredage_i} + \gamma_{\beta_{1_{SGA}}} x_{SGA_i} + \gamma_{\beta_{1_{ethnicity}}} x_{ethnicity} + \gamma_{\beta_{1_{parity}}} x_{parity_i} + \gamma_{\beta_{1_{BP}}} x_{BP_i} + \gamma_{\beta_{1_{diabetes}}} x_{diabetes_i} + \gamma_{\beta_{1_{smoking}}} x_{smoking_i} + \gamma_{\beta_{1_{maternalage}}} x_{maternalage_i} + \zeta_{\beta_{1_i}} \quad \text{(A.9)}$$

$$x_{SGA_i} = \gamma_0 + \gamma_{ethnicity} x_{ethnicity_i} + \gamma_{parity} x_{parity_i} + \gamma_{BP} x_{BP_i} + \gamma_{diabetes} x_{diabetes_i} + \gamma_{smoking} x_{smoking_i} + \gamma_{education} x_{education_i} + \gamma_{income} x_{income_i} + \gamma_{maternalage} x_{maternalage_i} + \zeta_{SGA_i} \quad \text{(A.10)}$$

$$x_{parity_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{parity_i} \quad \text{(A.11)}$$

$$x_{BP_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{BP_i} \quad \text{(A.12)}$$

$$x_{diabetes_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{diabetes_i} \quad \text{(A.13)}$$

$$x_{smoking_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{smoking_i} \quad \text{(A.14)}$$

$$x_{education_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{education_i} \quad \text{(A.15)}$$

$$x_{income_i} = \gamma_0 + \gamma_{maternalage} x_{maternalage_i} + \zeta_{income_i} \quad \text{(A.16)}$$

The equation for the quadratic term remained the same as the previous model (Model 2).

Conditional Model Adjusted for Early Life Modifiable Factors (Model 4):

The equation for BMI changed to reflect the addition of these factors as follows:

$$\begin{aligned} BMI_{it} = \ & \alpha_i + \beta_{1_i}\lambda_t + \beta_{2_i}\lambda_t^2 + \gamma_{matedu_{t_{cycles2to6}}} x_{matedu_{it_{cycles2to6}}} \\ & + \gamma_{income_{t_{cycles2to5}}} x_{income_{it_{cycles2to5}}} \\ & + \gamma_{activity_{t_{cycles3to5}}} x_{activity_{it_{cycles3to5}}} \\ & + \gamma_{screentime_{t_{cycles3to5}}} x_{screentime_{it_{cycles3to5}}} \\ & + \gamma_{sleep_{t_{cycles4to6}}} x_{sleep_{it_{cycles4to6}}} + \epsilon_{it} \end{aligned} \quad \text{(A.17)}$$

Equations for the mean intercept, linear slope, quadratic term, and other covariates remained the same as the previous model (Model 3).

Appendix B: Additional Model Results

Table B.1. Unconditional Model (Model 1)

	Females (N=635)				Males (N=597)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
α on Age Correction	-0.62	0.56	-1.10	0.270	-0.82	0.56	-1.46	0.145
β_1 on Age Correction	0.07	0.13	0.55	0.586	0.25	0.18	1.40	0.160
Variances								
BMI at 2 years	6.47	0.87	7.46	0.000	4.41	0.70	6.34	0.000
BMI at 4 years	5.76	0.71	8.11	0.000	4.99	0.67	7.46	0.000
BMI at 6 years	8.25	1.38	5.96	0.000	8.78	1.28	6.86	0.000
BMI at 8 years	10.34	2.97	3.49	0.000	6.87	1.11	6.21	0.000
BMI at 10 years	7.89	2.47	3.20	0.001	7.88	1.80	4.39	0.000

Table B.2. Conditional Model with SGA Term (Model 2)

	Females (N=635)				Males (N=597)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
α on Age Correction	-0.62	0.56	-1.11	0.267	-0.82	0.56	-1.46	0.145
β_1 on Age Correction	0.07	0.13	0.56	0.576	0.25	0.18	1.44	0.151
Variances								
BMI at 2 years	6.39	0.85	7.51	0.000	4.41	0.69	6.36	0.000
BMI at 4 years	5.72	0.70	8.19	0.000	4.98	0.67	7.44	0.000
BMI at 6 years	8.41	1.41	5.96	0.000	8.79	1.28	6.89	0.000
BMI at 8 years	10.32	2.95	3.49	0.000	6.92	1.11	6.21	0.000
BMI at 10 years	7.87	2.51	3.13	0.002	7.83	1.79	4.38	0.000

Table B.3. Conditional Model Adjusted for Prenatal and Early Life Sociodemographic and Maternal variables (Model 3)

	Females (N=435)				Males (N=403)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
α on Age Correction	-0.49	0.61	-0.80	0.424	-0.01	0.61	-0.01	0.994
α on Maternal Age	0.36	0.34	1.08	0.280	-0.37	0.33	-1.13	0.259
α on Parity	1.03	0.37	2.80	0.005	-0.12	0.33	-0.35	0.726
α on Blood Pressure	-0.54	0.51	-1.06	0.291	0.27	0.46	0.59	0.554
α on Diabetes	-2.61	0.52	-4.99	0.000	-0.43	0.49	-0.89	0.372
α on Smoking	0.26	0.46	0.56	0.577	1.21	0.45	2.72	0.006
α on Race	1.71	0.97	1.76	0.078	0.96	0.65	1.48	0.138
α on Education at C1	0.11	0.17	0.63	0.526	0.26	0.22	1.21	0.225
α on Income at C1	-0.07	0.15	-0.48	0.634	-0.05	0.14	-0.34	0.734
β_1 on Age Correction	0.03	0.13	0.26	0.794	0.20	0.16	1.24	0.215
β_1 on Maternal Age	-0.02	0.07	-0.25	0.801	-0.07	0.08	-0.84	0.398
β_1 on Parity	-0.09	0.08	-1.15	0.252	0.11	0.08	1.33	0.184
β_1 on Blood Pressure	0.19	0.12	1.65	0.098	-0.01	0.11	-0.08	0.933
β_1 on Diabetes	0.30	0.13	2.32	0.020	0.31	0.12	2.65	0.008
β_1 on Smoking	-0.04	0.11	-0.37	0.713	-0.07	0.09	-0.75	0.452
β_1 on Race	-0.31	0.21	-1.49	0.135	-0.24	0.18	-1.35	0.178
SGA on Maternal Age	0.04	0.05	0.69	0.492	0.04	0.04	0.91	0.365
SGA on Parity	-0.09	0.06	-1.48	0.138	-0.06	0.04	-1.47	0.141
SGA on Blood Pressure	0.10	0.08	1.29	0.196	0.05	0.06	0.94	0.347
SGA on Diabetes	0.12	0.14	0.84	0.404	-0.07	0.03	-2.44	0.015
SGA on Smoking	0.27	0.07	3.57	0.000	0.11	0.07	1.67	0.095
SGA on Race	-0.10	0.03	-2.84	0.004	-0.03	0.04	-0.71	0.480
SGA on Education at C1	-0.02	0.03	-0.91	0.361	-0.01	0.02	-0.61	0.542

Table B.3. Conditional Model Adjusted for Prenatal and Early Life Sociodemographic and Maternal variables (Model 3)

	Females (N=435)				Males (N=403)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
SGA on Income at C1	0.01	0.02	0.29	0.772	-0.01	0.01	-0.46	0.643
Parity on Maternal Age	0.37	0.07	5.14	0.000	0.21	0.10	2.17	0.030
Blood Pressure on Maternal Age	0.08	0.07	1.26	0.208	-0.05	0.04	-1.25	0.213
Diabetes on Maternal Age	0.08	0.06	1.37	0.171	0.01	0.03	0.45	0.655
Smoking on Maternal Age	0.03	0.07	0.46	0.648	-0.13	0.06	-2.22	0.027
Education at C1 on Maternal Age	0.09	0.20	0.46	0.649	0.82	0.14	5.82	0.000
Income at C1 on Maternal Age	0.78	0.13	6.04	0.000	0.64	0.18	3.63	0.000
BMI at 2 years on Education at C2	-0.10	0.26	-0.39	0.698	-0.19	0.29	-0.65	0.515
BMI at 2 years on Income at C2	0.08	0.29	0.27	0.790	0.00	0.23	-0.01	0.995
BMI at 4 years on Education at C3	0.25	0.27	0.92	0.357	-0.18	0.32	-0.58	0.561
BMI at 4 years on Income at C3	0.08	0.25	0.32	0.747	0.48	0.26	1.86	0.062
BMI at 6 years on Education at C4	-0.74	0.39	-1.90	0.057	-0.56	0.31	-1.80	0.072
BMI at 6 years on Income at C4	0.28	0.27	1.03	0.304	0.36	0.28	1.26	0.207
BMI at 8 years on Education at C5	-0.20	0.26	-0.77	0.441	-0.60	0.26	-2.29	0.022
BMI at 8 years on Income at C5	0.04	0.33	0.11	0.911	0.35	0.28	1.25	0.210
BMI at 10 years on Education at C6	-0.49	0.28	-1.77	0.076	-0.52	0.32	-1.62	0.106
BMI at C3 on PA at C3	-0.12	0.07	-1.85	0.064	-0.08	0.08	-0.90	0.367
BMI at C4 on PA at C4	0.03	0.12	0.25	0.805	-0.02	0.09	-0.24	0.809
BMI at C5 on PA at C5	0.08	0.08	1.00	0.318	-0.15	0.09	-1.70	0.089
BMI at C3 on TV at C3	-0.11	0.14	-0.78	0.437	-0.19	0.15	-1.31	0.191
BMI at C4 on TV at C4	0.11	0.39	0.29	0.772	-0.08	0.23	-0.35	0.726
BMI at C5 on TV at C5	-0.22	0.33	-0.68	0.495	-0.21	0.36	-0.59	0.555
BMI at C4 on Sleep at C4	0.02	0.19	0.09	0.930	0.04	0.18	0.24	0.812

Table B.3. Conditional Model Adjusted for Prenatal and Early Life Sociodemographic and Maternal variables (Model 3)

	Females (N=435)				Males (N=403)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
BMI at C5 on Sleep at C5	-0.30	0.26	-1.16	0.247	-0.33	0.25	-1.29	0.197
BMI at C6 on Sleep at C6	-0.07	0.27	-0.25	0.799	-0.01	0.29	-0.03	0.976
Variances								
BMI at 2 years	5.32	0.76	7.00	0.000	4.23	0.80	5.29	0.000
BMI at 4 years	5.43	0.76	7.12	0.000	5.27	0.77	6.86	0.000
BMI at 6 years	7.89	1.42	5.58	0.000	7.66	1.21	6.32	0.000
BMI at 8 years	7.60	1.19	6.40	0.000	6.18	1.00	6.16	0.000
BMI at 10 years	4.61	1.09	4.25	0.000	6.25	1.36	4.61	0.000
SGA	0.10	0.02	5.68	0.000	0.06	0.01	4.57	0.000
Parity	0.22	0.01	16.88	0.000	0.24	0.01	21.94	0.000
Blood Pressure	0.09	0.02	4.95	0.000	0.10	0.02	5.87	0.000
Diabetes	0.04	0.01	2.48	0.013	0.05	0.01	3.87	0.000
Smoking	0.17	0.02	9.85	0.000	0.17	0.02	9.68	0.000
Education at C1	1.12	0.11	10.32	0.000	0.87	0.08	11.11	0.000
Income at C1	0.78	0.07	10.53	0.000	0.81	0.08	10.09	0.000

Table B.4. Conditional Model Adjusted for Early Life Modifiable Factors (Model 4)

	Females (N=408)				Males (N=371)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Covariances								
Education at C5 with Sleep at C6	Covariance between these variables was fixed to zero to allow for model convergence.							
Regression Coefficients								
α on Age Correction	-0.28	0.61	-0.46	0.647	-0.21	0.62	-0.34	0.735
α on Maternal Age	0.27	0.35	0.78	0.437	-0.25	0.32	-0.77	0.439
α on Parity	0.97	0.37	2.61	0.009	-0.14	0.33	-0.42	0.678
α on Blood Pressure	-0.44	0.55	-0.80	0.422	0.37	0.45	0.82	0.410
α on Diabetes	-2.81	0.51	-5.57	0.000	-0.61	0.51	-1.19	0.234
α on Smoking	0.39	0.47	0.83	0.407	1.28	0.46	2.78	0.006
α on Race	1.69	0.91	1.86	0.063	0.75	0.65	1.15	0.250
α on Education at C1	0.07	0.18	0.40	0.686	0.30	0.24	1.24	0.216
α on Income at C1	0.01	0.15	0.04	0.968	-0.03	0.14	-0.22	0.823
β_1 on Age Correction	0.03	0.13	0.22	0.826	0.22	0.16	1.38	0.168
β_1 on Maternal Age	-0.07	0.09	-0.77	0.440	-0.11	0.08	-1.37	0.170
β_1 on Parity	-0.05	0.08	-0.61	0.543	0.09	0.08	1.17	0.244
β_1 on Blood Pressure	0.12	0.13	0.93	0.355	-0.03	0.12	-0.22	0.826
β_1 on Diabetes	0.59	0.27	2.20	0.028	0.35	0.12	2.81	0.005
β_1 on Smoking	-0.02	0.12	-0.18	0.857	-0.04	0.10	-0.38	0.705
β_1 on Race	-0.29	0.19	-1.49	0.137	-0.23	0.18	-1.24	0.215
SGA on Maternal Age	0.05	0.06	0.91	0.362	0.03	0.05	0.71	0.475
SGA on Parity	-0.10	0.06	-1.63	0.102	-0.08	0.05	-1.76	0.078
SGA on Blood Pressure	0.12	0.09	1.35	0.177	0.05	0.06	0.85	0.395

Table B.4. Conditional Model Adjusted for Early Life Modifiable Factors (Model 4)

	Females (N=408)				Males (N=371)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Regression Coefficients								
SGA on Diabetes	0.04	0.15	0.30	0.767	-0.06	0.03	-2.14	0.033
SGA on Smoking	0.26	0.08	3.39	0.001	0.13	0.08	1.74	0.082
SGA on Race	-0.10	0.04	-2.77	0.006	-0.03	0.05	-0.73	0.466
SGA on Education at C1	-0.02	0.03	-0.81	0.416	-0.02	0.02	-0.80	0.426
SGA on Income at C1	0.01	0.03	0.26	0.795	-0.01	0.02	-0.71	0.479
Parity on Maternal Age	0.36	0.08	4.59	0.000	0.17	0.11	1.63	0.104
Blood Pressure on Maternal Age	0.07	0.07	1.04	0.300	-0.06	0.04	-1.36	0.175
Diabetes on Maternal Age	0.05	0.06	0.85	0.397	-0.01	0.03	-0.35	0.727
Smoking on Maternal Age	0.04	0.07	0.49	0.623	-0.10	0.06	-1.85	0.064
Education at C1 on Maternal Age	0.09	0.22	0.40	0.691	0.64	0.13	4.75	0.000
Income at C1 on Maternal Age	0.81	0.13	6.24	0.000	0.64	0.20	3.13	0.002
BMI at 2 years on Education at C2	-0.21	0.28	-0.75	0.454	-0.19	0.30	-0.61	0.540
BMI at 2 years on Income at C2	0.12	0.30	0.39	0.700	-0.05	0.23	-0.19	0.846
BMI at 4 years on Education at C3	0.36	0.29	1.24	0.216	-0.23	0.31	-0.74	0.459
BMI at 4 years on Income at C3	0.08	0.26	0.32	0.749	0.33	0.25	1.33	0.183
BMI at 6 years on Education at C4	-0.72	0.49	-1.48	0.140	-0.63	0.32	-1.94	0.052
BMI at 6 years on Income at C4	0.24	0.29	0.82	0.413	0.30	0.28	1.10	0.270
BMI at 8 years on Education at C5	-0.33	0.27	-1.24	0.215	-0.68	0.27	-2.49	0.013
BMI at 8 years on Income at C5	-0.04	0.35	-0.11	0.914	0.32	0.29	1.10	0.273
BMI at 10 years on Education at C6	-0.48	0.29	-1.69	0.092	-0.69	0.32	-2.17	0.030

Table B.4. Conditional Model Adjusted for Early Life Modifiable Factors (Model 4)

	Females (N=408)				Males (N=371)			
	Estimate	**S.D.**	**Est./S.D.**	**p-value**	**Estimate**	**S.D.**	**Est./S.D.**	**p-value**
Variances								
BMI at 2 years	5.70	0.86	6.67	0.000	4.20	0.79	5.31	0.000
BMI at 4 years	5.51	0.76	7.25	0.000	5.06	0.78	6.50	0.000
BMI at 6 years	7.96	1.46	5.44	0.000	7.90	1.25	6.31	0.000
BMI at 8 years	7.22	1.21	5.97	0.000	5.92	0.94	6.29	0.000
BMI at 10 years	5.17	1.32	3.92	0.000	5.42	1.29	4.21	0.000
SGA	0.10	0.02	5.56	0.000	0.06	0.01	4.84	0.000
Parity	0.22	0.01	17.14	0.000	0.24	0.01	23.71	0.000
Blood Pressure	0.09	0.02	4.46	0.000	0.10	0.02	5.66	0.000
Diabetes	0.04	0.02	2.52	0.012	0.04	0.01	3.55	0.000
Smoking	0.17	0.02	10.03	0.000	0.16	0.02	8.50	0.000
Education at C1	1.13	0.11	10.10	0.000	0.80	0.08	10.51	0.000
Income at C1	0.74	0.08	9.88	0.000	0.82	0.09	9.29	0.000
Education at C5	1.17	0.10	11.90	0.000	1.03	0.09	11.00	0.000
Sleep at C6	0.81	0.07	11.31	0.000	0.81	0.09	9.19	0.000

Appendix C: Variable Dictionary

Table C.1. Variable Dictionary

Variable Name	NLSCY variable(s)	Coding utilized for analyses
Age (Cycles 1 to 6)	**a**mmcdq1b` to **f**mmcdq1b	Continuous (years)
Birth weight	amdcq13b	Continuous (grams)
Birth length	amdcq14b	Continuous (m)
BMI at each cycle	height weight	Continuous (weight in kg/height in m^2)
Gender	ammcq02	0 (Females) 1 (Males)
Gestational age	amdcd06	Continuous (weeks)
Height (Cycles 2 to 6)	**b**hlcq03b to **f**hlcq03b	Continuous (m)
Income Adequacy (Cycles 1 to 5)	**a**inhd07 to **e**inhd07	0 = lowest 1 = lower middle 2 = middle 3 = upper middle 4 = highest
Maternal age	admcd18	Continuous (years)
Maternal schooling (Cycles 1 to 4, 5, 6)	**a**edpd02 to **d**edpd02, eedped02, fedped02	0 = less than secondary 1 = secondary school graduation 2 = beyond high school 3 = college or university degree (including trade school)
Parity	ahlmq09	0 = one past pregnancy 1 = more than one past pregnancy

Table C.1. Variable Dictionary

Variable Name	NLSCY variable(s)	Coding utilized for analyses
Physical activity frequency (Cycles 3 to 5)		
Organized PA like gymnastics or martial arts *Organized PA except gymnastics or martial arts* *Unorganized PA without a coach*	**c**accb3aa to **e**accb3aa **c**accq3a to **e**acce3a **c**accq3b to **e**accq3b	0 = almost never 1 = about once a month 2 = about once a week 3 = few times a week 4 = most days
Physical activity additive score	Cycle 3: caccb3aa + caccq3a + caccq3b Cycle 4: daccb3aa + daccq3a + daccq3b Cycle 5: eaccb3aa + daccq3a + eaccq3b	Continuous (from 0 to 12)
Pregnancy hypertension	amdcq01b	0 = no 1= yes
Pregnancy smoking	amdcq03	0 = no 1= yes
Race	bsdpb4a**a** to bsdpb4a**l**	0 = white 1= non-white or bi-racial
Sample weight variable	bwtcw01c	Continuous (bwtcw01c ÷ $\overline{bwtcw01c}$; N=1,273)
SGA Status	amdcq13b amdcd06	0 (AGA: birth weight ≥10th %ile and <90th %ile for gestational age and gender) 1 (SGA: birth weight <10th %ile for gestational age and gender) *%iles based on reference charts by Kramer et al.*[150]

Table C.1. Variable Dictionary

Variable Name	**NLSCY variable(s)**	**Coding utilized for analyses**
Singleton status	amdcq15	0 (Singleton) 1 (Child of multiple birth)
Sleep Duration (Cycles 3 to 5)	**d**slcdq7 to **f**slcdq7	Continuous (hours)
Television Use (Cycles 3 to 5)	**c**acccq4b to **e**acccq4b	Continuous (hours)
Weight (Cycles 2 to 6)	**b**hlcq04a to **f**hlcq04a	Continuous (kg)

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