The Effects of Physical Activity and Sedentary Behavior Across Pregnancy on Early Childhood Growth and Development

by

Melissa A Jones

Bachelor of Science, Saginaw Valley State University, 2016

Master of Science, University of Pittsburgh, 2017

Submitted to the Graduate Faculty of the

School of Education in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2020

UNIVERSITY OF PITTSBURGH

SCHOOL OF EDUCATION

This dissertation was presented

by

Melissa A Jones

It was defended on

August 7, 2020

and approved by

Kelliann Davis, Associate Professor, Health and Human Development

Sharon Ross, Associate Professor, Health and Human Development

Klaus Libertus, Assistant Professor, Psychology

Dissertation Director: Bethany Barone Gibbs, Associate Professor, Health and Human Development

The Effects of Physical Activity and Sedentary Behavior across Pregnancy on Early Childhood Growth and Development

Melissa A. Jones, PhD

University of Pittsburgh, 2020

There is evidence to support that early life exposures are related to health outcomes across the lifespan. Whether maternal activity behaviors during pregnancy may impact early childhood health remains unknown. **Methods**: This follow-up study recruited mothers with objective measurement of sedentary behavior and MVPA across pregnancy from a previous cohort study. Offspring anthropometrics from all pediatric visits from birth to 24 months were abstracted from children's medical records (n=60). Motor development was parent-reported on the Early Motor Questionnaire (EMQ) and by age of crawling and walking onset (n=70). Childhood growth was analyzed as dichotomous catch-up growth (increase in BMI z-score >2.0 between birth and 12-months) and growth rate (incremental rate of BMI z-score change up to 24-months). Logistic regression models examined the associations of maternal activity with risk for catch-up growth. Mixed linear models examined associations of maternal activity with growth rate. Linear regression models examined the associations between maternal activity and EMQ scores, crawling, and walking onset age. Maternal activity was the independent variable in all models and analyzed in two ways: trimester-specific and across pregnancy using trajectory groups. Adjustment for BMI z-score at birth was added to each model to evaluate whether birth size attenuated associations. **Results:** Higher maternal MVPA was related to a greater risk for catch-up growth ($p<0.03$), more rapid growth ($p<0.02$), more advanced motor development ($p<0.03$) and, in the second trimester only, later age of crawling onset ($p=0.048$). Higher maternal sedentary time was related to more

rapid growth rate (p=0.001) but not catch-up growth or motor development. Associations between maternal MVPA and catch-up growth were attenuated by adjustment for BMI z-score at birth, while associations of MVPA with motor development were unchanged. **Conclusion:** Our findings identify a modifiable prenatal exposure which may impact health risk of the offspring. While MVPA may improve motor development in early childhood, the increased risk for catch-up growth elicits further investigation. Higher sedentary behavior being related to more rapid childhood growth reinforces the need for more sedentary behavior research and consideration of recommendations for pregnant women. Overall, maternal activity profile shows promise as a modifiable behavior to improve intergenerational health.

Table of Contents

1.0 Introduction **1**

1.1 Background **1**

1.2 Specific Aims **4**

1.3 Signficance and Rationale **5**

2.0 Review of the Literature **8**

2.1 Developmental Origins of Health and Disease **8**

2.1.1 Maternal Activity Profile During Pregnancy **12**

2.1.2 Maternal Activity Profile and Birth Size **13**

2.1.3 Maternal Activity Profile and Early Childhood Growth **16**

2.1.4 Maternal Activity Profile and Motor Development **18**

2.2 Short and Long-Term Offspring Health **20**

2.2.1 Cardiovascular Health **21**

2.2.2 Metabolic Health **22**

2.2.3 Adiposity and Body Size **23**

2.2.4 Childhood Motor Development **24**

2.2.5 Implications of Large Birth Size **25**

2.3 Physiological Mechanisms **26**

2.3.1 Placental **26**

2.3.2 Structural: Animal Studies **27**

2.3.3 Structural: Human Studies **28**

2.4 Role of Social Determinants in Developmental Origins of Health and Disease **28**

2.5 Conclusion 31

3.0 Methods 33

3.1 Study Design 33

3.2 Sample Population 34

3.3 Assessment Procedures 36

3.3.1 Maternal Activity During Pregnancy 37

3.3.2 Infant Birth Size and Growth Pattern 38

3.3.3 Questionnaires 38

3.4 Power Considerations 40

3.5 Statistical Analysis 41

4.0 Results 43

4.1 Study Participants 43

4.1.1 Recruitment and Enrollment 43

4.1.2 Participant Characteristics 44

4.2 Specific Aim 1 46

4.2.1 Catch-up Growth 46

4.2.2 Growth Rate 48

4.3 Specific Aim 2 50

4.3.1 Early Motor Questionnaire 51

4.3.2 Crawling and Walking Onset 55

4.4 Exploratory Aim 56

4.4.1 Catch-Up Growth 57

4.4.2 Motor Development 58

5.0 Discussion **60**

5.1 Summary of Findings **60**

5.2 Catch-Up Growth and Growth Rate **61**

5.3 Motor Development **65**

5.4 Strengths and Limitations **70**

5.5 Future Directions **71**

5.6 Conclusions **73**

Appendix A Recruitment Flyer **74**

Appendix B Screening Form **75**

Appendix C Demographic and Health Questionnaires **76**

Appendix D Breastfeeding Questionnaires **79**

Appendix E Early Motor Questionnaire **81**

Appendix F Walking and Crawling Onset **88**

Appendix G Supplemental Tables **89**

Bibliography **93**

List of Tables

Table 1 Study Inclusion and Exclusion Criteria 35

Table 2. Maternal and Child Characteristics Overall and by Activity Trajectories..... 45

Table 3. Odds of BMI Z-score Catch-up Growth by Maternal Sedentary Behavior and MVPA Trajectories..... 47

Table 4. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months by Trimester-Specific Maternal Sedentary Behavior and MVPA 48

Table 5 Incremental Rate of BMI Z-Score Change with Age by Trimester Specific Maternal Sedentary and MVPA..... 50

Table 6. Association of EMQ Domains with Maternal Sedentary and MVPA by Trajectory Groups..... 52

Table 7 Association of EMQ Domains with Trimester Specific Maternal Sedentary and MVPA..... 54

Table 8. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months of Age by Maternal Sedentary and MVPA Trajectory With and Without Adjustment for BMI Z-Score at Birth..... 57

Table 9. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months of Age by Trimester Specific Activity With and Without Adjustment for BMI Z-Score at Birth 58

Table 10. Associations Between Activity Trajectories and EMQ Scores With and Without Adjustment for BMI Z-Score at Birth 59

List of Figures

Figure 1. Hypothesized Relationship Between Maternal Activity, Fetal Growth, and Early Childhood Health 7

Figure 2. David Barker's Landmark Study Associating Low Birth Weight Mortality with Ischemic Heart Disease Mortality 9

Figure 3. Peter Gluckman's Mismatch Concept 11

Figure 4. Maternal MVPA and Sedentary Behavior Trajectories 15

Figure 5. Ponderal Index by MVPA and Sedentary Behavior Trajectory Group..... 16

Figure 6 Diagram of Participant Enrollment in the MoM Health 2.0 Study 44

Figure 7. Incremental Rate of BMI Z-Score Change by Sedentary and MVPA Trajectory 49

Figure 8. Predicted EMQ Scores by Activity Trajectories 53

Figure 9. Predicted Age of Crawling and Walking Onset by Activity Trajectories 56

1.0 Introduction

1.1 Background

Non-communicable diseases, such as cardiovascular disease and type 2 diabetes, are highly prevalent. In the United States, 121 million and 26 million individuals have been diagnosed with cardiovascular disease and diabetes, respectively.[1] Globally, one in four deaths are a result of a non-communicable diseases.[2] These diseases develop across the lifespan[3] and, therefore, preventative efforts are critically important.

The Developmental Origins of Health and Disease theory focuses on the fetal environment as the earliest determinant of long-term, non-communicable disease risk. A suboptimal fetal environment results in poor fetal growth and increased susceptibility to disease development across the lifespan.[4-6] Birth size is often used as proxy measure of adequacy of nutrient delivery and subsequent fetal development and is represented as birthweight (grams), weight-for-length (such as ponderal index= birthweight(g)*100/birth length(cm)^3 or body mass index= birthweight(kg)/birth length(m)^2), or size for gestational age (based on population norms and classified as small, adequate, or large for gestational age).[7] A smaller birth size has repeatedly been linked to poorer health outcomes in childhood and adulthood. These include higher blood pressure, insulin, and body weight in childhood,[8-11] and greater risk for ischemic heart disease, coronary artery disease, hypertension, and type 2 diabetes in adulthood.[12-16]

To prevent this cascade of cardiovascular risk that begins *in utero*, improved understanding of modifiable factors that impact the intrauterine environment are needed to inform intervention targets and public health recommendations for pregnant women. Nutrients obtained and

sufficiency of fetal growth is a result of the environment in which the fetus is growing.[17] The placenta responds to maternal nutrition, obesity, inflammation, and other perturbations, determining the intrauterine environment.[17] Thus, through an effect on the placenta, maternal health behaviors during pregnancy may play an important role in fetal programming of disease and provide opportunity for future interventions.

One potential behavioral target for improving the fetal environment is maternal activity profile during pregnancy, including moderate-to-vigorous intensity physical activity (MVPA) and sitting (i.e., sedentary behavior). This profile may have an effect on fetal growth due to the effect of exercise on placental nutrient transport and energy metabolism.[18,19] Higher levels of MVPA have been associated with improved fetal growth[20-24] and early childhood neuromotor development.[25] Less is known about the potential effects of sedentary behavior, defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture, on fetal growth.[26] Few studies have examined the associations between sedentary behavior and fetal growth. The existing studies have found no association between sedentary behavior and size at birth; however, these studies have measured sedentary behavior by self-report,[27,28] which likely has significant error in measurement, or only report birth weight[29,30] as an outcome, which may not capture the effects of growth restriction as a weight-for-length measure would. Intriguing pilot data from a recent study in our lab (n=103) support a potential effect of sedentary behavior on fetal growth. This study found that high levels of objectively-measured sedentary time during pregnancy were related to lower (worse) infant ponderal index at birth ($p<0.001$). In the same study, maternal MVPA patterns were not related to infant ponderal index. These findings provide more robust evidence that the sedentary behavior component of the maternal activity profile might be associated with fetal health and development

Overall, it appears maternal activity profile could be important for fetal growth and development, but limited data are currently available. Yet, to our knowledge, no prior research has assessed the longitudinal effects of sedentary behavior during pregnancy on child outcomes during early childhood; this research question is the focus of the current dissertation project.

In early life (<24 months old), markers of cardiometabolic disease development (e.g., elevated blood pressure, reduced insulin sensitivity) may not yet be apparent. However, infant growth rate and early motor development have been identified as important early life health indicators. There is substantial evidence demonstrating the long-term impact of accelerated growth in early life.[31,32] Infants with lower birth weight, lower weight-for-length, or those born small for gestational age (SGA) are at a greater risk for rapid growth in the first 2 years of life.[33] Children who grow more rapidly have greater risk for poor cardiometabolic health and overweight and obesity in childhood and adulthood.[10,31-35] Less is known about the long-term health implications of motor development at a young age; however, there is evidence to support its utility. Poorer or delayed motor development is related to increased risk for obesity and lower levels of MVPA[36,37] in childhood.[38]

Though our previous data suggest maternal sedentary behavior is associated with infant size at birth, whether the effects of maternal activity profile across pregnancy persist after birth to impact growth and development of the offspring in early life remains unknown. Thus, the present study includes longitudinal follow-up study of the children born to mothers enrolled in our previous cohort study which measured objective activity patterns across each trimester of pregnancy. This project measured new outcomes including early childhood growth (Aim 1) and development (Aim 2) at 1-2 years of age to relate to maternal activity profile during pregnancy. An additional exploratory aim sought to evaluate whether previously identified effects of sedentary

behavior on birth size attenuated associations identified in the first two aims. Therefore, the aims of the current investigation were as follows:

1.2 Specific Aims

Specific Aim 1: To examine associations between maternal activity profile across pregnancy and by trimester with infant growth rate up to 24-months of life.

Hypothesis: Higher maternal sedentary behavior and lower maternal MVPA will be related to greater risk of catch-up growth and more rapid growth rate.

Specific Aim 2: To examine associations between maternal activity profile across pregnancy and by trimester with child motor development.

Hypothesis: Lower maternal sedentary behavior and higher maternal MVPA will be related to more advanced motor development.

Exploratory Aim: To evaluate the influence of BMI z-score at birth on associations observed in Aims 1 and 2.

Hypothesis: Covariate adjustment for BMI z-score will attenuate the associations between maternal activity profile and early childhood growth and motor development.

1.3 Significance and Rationale

Previous studies have found that activity during pregnancy is associated with improved nutrient delivery to the fetus by improving the function of the placenta.[19,39] In conjunction with our findings that high sedentary time was related to lower birth size, we hypothesized that maternal activity profile influenced the risk for insufficient nutrients or growth restriction in our cohort. Previous research, primarily in animal models, has demonstrated sustained structural and functional difference in organ systems resulting from growth restriction during gestation. These studies have found poorer metabolic function,[40] blood pressure regulation, and cardiovascular function.[41,42] In humans, reduced neurodevelopment[43] and narrowed carotid artery structure in children[44] was found in those that were growth restricted *in utero*. One early sign of insufficient intrauterine environment or growth restriction includes rapid growth during early childhood,[10,11] which is strongly related to long-term cardiometabolic risk[12,45-47] and adiposity.[11,48] Therefore, preventing fetal growth restriction and subsequent rapid growth patterns is critical to improve long-term health across the lifespan.

This present study tested the hypothesis that more favorable maternal activity profile during pregnancy was associated with intermediate outcomes between birth and cardiometabolic disease in adulthood. These outcomes included risk of catch-up or rapid growth and motor-skill development between 12-24 months old. With strong evidence supporting the Developmental Origins of Health and Disease, understanding how modifiable behaviors in pregnancy may impact child health risk is crucial step to improve population health.

According to the American College of Obstetrics and Gynecology, pregnant women who are free of complications are recommended to participant in 20-30 minutes of MVPA on most days of the week.[49] However, data from the National Health and Nutrition Examination Survey

(NHANES) 2003-2006, using objectively-measured activity from waist-worn accelerometry, estimates that pregnant women accumulate only 12 minutes of MVPA per day and spend 7 hours per day sedentary.[50] The high prevalence of inactivity and sedentary behavior among pregnant women provides an opportunity for behavioral intervention.

It is important to note that one lifestyle behavior is not solely responsible for alterations in fetal growth and development. Our conceptual framework in **Figure 1** highlights various modifiable and non-modifiable factors that may contribute to maternal activity, the intrauterine environment, and risk for rapid growth or developmental delay in the offspring. Sufficiency of nutrient delivery is dependent on the intrauterine environment which is determined by a number of these maternal factors.[6,51,52] These include low socioeconomic status[53] and minoritized race or ethnicity,[54] both of which have been associated with poor maternal-fetal outcomes. Additionally, feeding type (breastfeeding or formula fed), primary caregiver, and maternal diet all impact childhood health.[55] Our study's focus on activity profile during pregnancy as it relates to infant outcomes (bolded sections of **Figure 1**), while measuring these other important covariates, will help to determine if activity may be a target for future interventions to improve the fetal environment and subsequent growth and development in childhood.

The present study aimed to address whether women who participate in more sedentary behavior and/or less MVPA have babies at a greater risk for rapid growth and slower motor development. These findings could inform the basis for sedentary behavior or MVPA interventions and recommendations during pregnancy to potentially affect the health of future generations.

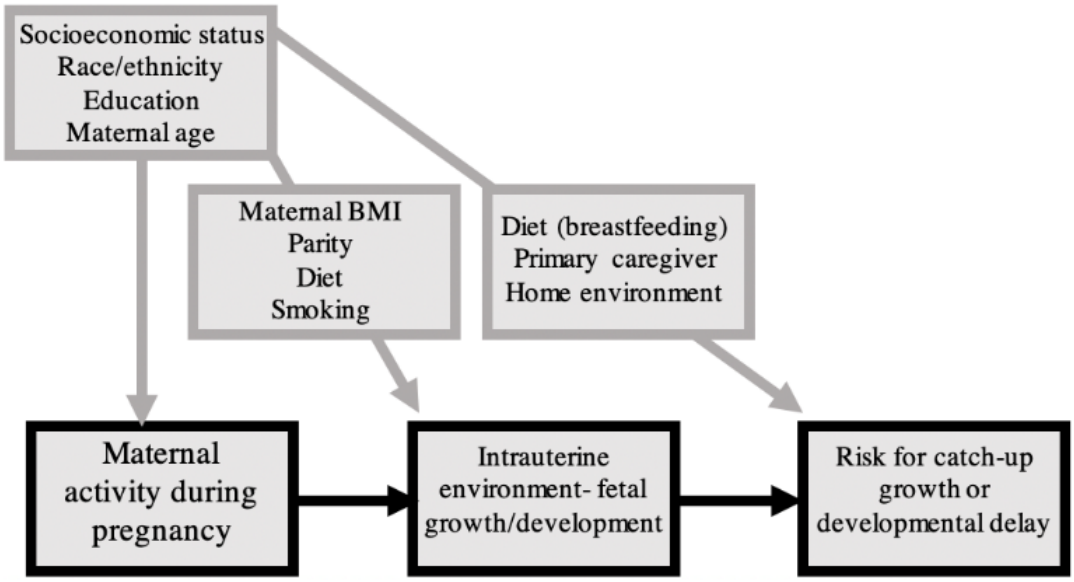

Figure 1. Hypothesized Relationship Between Maternal Activity, Fetal Growth, and Early Childhood Health

2.0 Review of the Literature

2.1 Developmental Origins of Health and Disease

The Developmental Origins of Health and Disease theory was developed by David Barker (originally coined the "Barker Hypothesis"). Barker was the first to link early life fetal environment to the development of chronic disease when he observed that geographical areas with higher infant mortality from low birth weight also had higher rates of ischemic heart disease.[56] Observed associations between infant mortality and ischemic heart disease mortality ratios can be seen in **Figure 2**. In several later cohort studies, Barker found the same association in which lower birthweight, or lower ponderal index (an indicator of thinness), were associated with a greater risk of cardiometabolic diseases in adulthood.[13,14,45]

Much of this research was established during the time of the Dutch hunger winter, a famine occurring in the German-occupied Netherlands during World War II. These difficult circumstances created a natural experiment to examine the effects of famine on fetal development. Among those exposed to famine, maternal malnutrition during pregnancy was related to an increased risk for cardiovascular disease of the offspring in adulthood.[16] This all led to the hypothesis, and the basis of the Developmental Origins of Health and Disease theory, that the intrauterine environment programs future health and disease risk.[15]

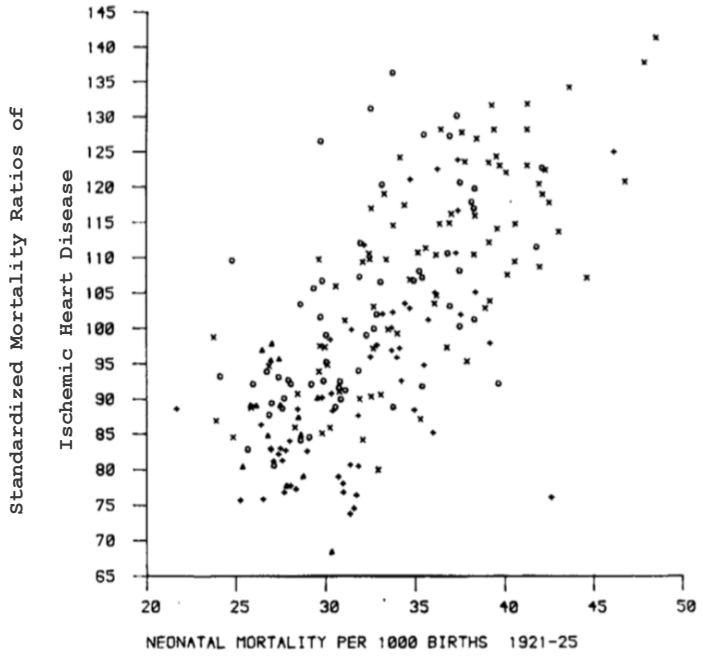

Figure 2. David Barker's Landmark Study Associating Low Birth Weight Mortality with Ischemic Heart Disease Mortality

Programming is a process by which the fetal environment, determined by fetal under- or over-nutrition, hormones, and placental function, affects the structure and physiology of cells and organs in offspring. This process occurs *in utero* then modifies lifelong health and disease susceptibility.[4,15] Induced growth restriction of fetuses in animal models has demonstrated persisting changes to metabolic and organ function of offspring such as increased blood pressure and cholesterol, and reduced insulin sensitivity.[57,58] In humans, low birth weight, SGA, or low weight-for-length measures like BMI or ponderal index (birthweight (g)*100/birth length(m)^3) are used as indicators of growth restriction *in utero*. However, weight-for-length measures are considered better indicators of growth restriction as they measure of thinness at birth with length (height) considered, rather than weight alone.[7,59,60] Based on the theory, babies exposed to a poor fetal environment, resulting in growth restriction and low weight-for-length measures at birth, are programmed with an increased risk of developing cardiometabolic disease over their lifetime.

Nutrients obtained and sufficiency of fetal growth is a result of the environment in which the fetus is growing.[17] The *in utero* environment is determined by the placenta, a metabolically active and changing tissue. One review indicates that "changes in placental nutrient transport may influence fetal nutrient availability, which determines fetal growth and body composition, and thus may link maternal perturbations to fetal programming." These maternal perturbations may include nutrition, diabetes, obesity, and inflammation.[17] Nutrition alters the placental function through a mechanism known as placental nutrient sensing. Through this mechanism, the placenta responds to nutritional cues from the mother and downregulates transport to the fetus when nutrients are deficient, resulting in fetal undernutrition and growth restriction. This review also notes that "fetal growth is matched to the ability of the maternal supply line to allocate resources to the fetus."[61]

Further, inflammatory markers in the placenta can also affect fetal growth. Pregnant women with overweight or obesity experience higher levels of chronic inflammation during the early stages of pregnancy.[62] Animal models have demonstrated the programming of metabolic dysfunction in offspring born to obese mice with elevated inflammatory markers in the placenta.[63] Lastly, gestational diabetes (GDM) affects fetal growth through the nutrient-sensing mechanism of the placenta. However, in this case, nutrients are delivered in excess due to the poor regulation of glucose. This effect is seen even within "normal" glucose levels with higher blood glucose contributing to excessive fetal growth even without overt GDM.[64]

The susceptibility of a fetus exposed to a poor intrauterine environment to future disease development is partly explained by the 'mismatch theory.'[65] During gestation, the fetus develops to survive in the environment it is growing in. An abnormal, nutrient-poor fetal environment followed by plentiful nutrients after birth is thought to result in a physiological mismatch and, thus, can increase susceptibility to chronic disease development.[66] This theory was first proposed by

Peter Gluckman in a book titled "Mismatch: How Our World No Longer Fits Our Bodies."[67] Animal models were used to compare nutrient deficiency during pregnancy and *ad libitum* nutrient intake after birth. The animals with matched prenatal and postnatal nutrient availability (both nutrient restricted or *ad libitum*) had better metabolic health compared to those mismatched (restricted in utero, *ad libitum* postnatal and vice versa).[65] The theoretical framework for this model can be found in **Figure 3.**

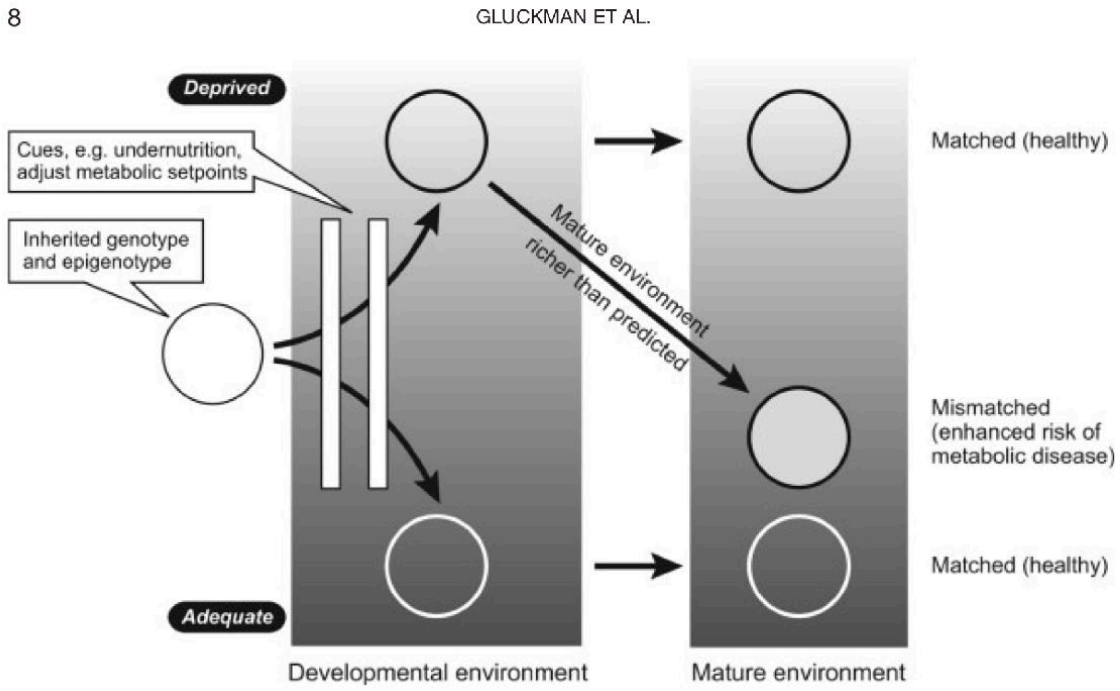

Figure 3. Peter Gluckman's Mismatch Concept

Though most research on the Developmental Origins of Health and Disease theory has focused on maternal nutrition, obesity, and metabolic dysfunction, the role of maternal activity on fetal growth has been less extensively studied. It is hypothesized that activity may have an effect on fetal growth because of the role activity plays in glucose and energy metabolism[18] and nutrient transport in the placenta.[19] This inconsistency in nutrient delivery may affect fetal growth, pre- and post-natal development, and subsequent cardiometabolic health.

2.1.1 Maternal Activity Profile During Pregnancy

According to NHANES (2003-2006), pregnant women spend an average of 12 minutes per day in MVPA and roughly 7 hours per day of the day in sedentary behavior.[50] The American College of Obstetrics and Gynecology recommends 20-30 minutes of MVPA on most days of the week for women with uncomplicated pregnancies to optimize maternal and fetal health outcomes.[49] The Department of Health and Human Services recently released guidelines for physical activity during pregnancy and postpartum that are in line with previous recommendations with respect to recommended levels of activity (i.e., 150 minutes per week of MVPA). The accompanying report also summarized that only 1 in 4 pregnant women are sufficiently active and that physical activity during pregnancy reduces the risk for excessive gestational weight gain, GDM, and postpartum depression.[68]

Unlike MVPA, there are no recommendations for sedentary behavior during pregnancy. Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture.[26] Sedentary behavior is independent of MVPA as a risk factor for poor health in the general adult population,[69] and meeting physical activity recommendations does not decrease sedentary time in pregnant women.[70] Therefore it is important to consider the effects of sedentary behavior in addition to MVPA during pregnancy on maternal and fetal health.

Below, the available literature on the effects of maternal activity profiles on infant birth size, childhood growth, and development will be discussed to elucidate the current understanding

and research gaps around the role of maternal activity profile in the Developmental Origins of Health and Disease.

2.1.2 Maternal Activity Profile and Birth Size

The primary fetal outcome assessed in studies of MVPA during pregnancy is birth size. This is typically expressed in one of three ways: birth weight (g), birth weight-for-length (i.e., ponderal index or BMI) or birth weight for gestational age. Birth weight for gestational age is based on population norms with $<10^{th}$ or $>90^{th}$ percentiles classified as small and large for gestational age, respectively. All births between the 10^{th} and 90^{th} percentiles are considered adequate for gestational age.[71]

The evidence has strongly and consistently associated MVPA during pregnancy with reduced risk for large for gestational age (LGA) newborn without increased risk for small for gestational age (SGA). There are currently five meta-analyses that have reached this conclusion.[20-24] In one of these meta-analysis with the most rigorous design criteria (only including randomized control trials with at least one supervised aerobic exercise session every two weeks), the pooled odds for a LGA newborn were 31% lower in the exercise vs. control groups, with no significant effect on odds of SGA or gestational age at delivery.[24] One meta-analysis assessed the timing of exercise during pregnancy based on self-reported activity and found that MVPA in late pregnancy was associated with lower risk for LGA, lower ponderal index, and no change in risk of SGA. There was no significant association with MVPA performed during early pregnancy and birth size.[72] Only one other meta-analysis mentions fetal body composition or weight-for-length and this study reported no association with maternal MVPA.[21] This is a limitation of the current literature as these measures are better indicators of growth restriction than birth weight or size for

gestational age[73] and therefore, additional benefits of MVPA on growth restriction may be present but have not yet been extensively studied.

In contrast, associations of sedentary behavior during pregnancy and birth size have not been well studied. Of the existing published studies, no significant associations have been found, though this may be attributable to the measurements used in these studies. One study used self-reported pre-pregnancy and early pregnancy sedentary behavior and found no association with birthweight, gestational age at delivery, or ponderal index.[28] However, these data may be less than valid since, contrary to NHANES data where pregnant women spent about 7 hours per day in sedentary behavior, women in this study only reported 2.5 hours per day of sedentary time. Another study finding no association used a retrospective case-control design that utilized recall of second trimester MVPA and sedentary time in matching cases of intrauterine growth restriction or low-birthweight with normal-weight infant controls.[27]

Conclusions from these studies are also weak since they also used poor methodology for measuring sedentary behavior. Research from our group has shown that that self-report of sedentary time during pregnancy is poorly correlated to objectively-measured sedentary time, with correlations typically ranging from 0.2-0.4.[74] The associations of birth size and objectively-measured sedentary behavior using 24-hour waist-worn Actigraph accelerometry was measured in two cohort studies. The first measured sedentary behavior at 15 weeks and 32 weeks gestation (n=111) and found no association between sedentary behavior at 15 weeks or change in sedentary behavior from 15 to 32 weeks with maternal reported birthweight.[29] A second study, which measured sedentary behavior at 16 weeks gestation in n=97 women, found no association between second trimester sedentary time and birth weight, though the association was in the expected direction with higher sedentary time related to lower birth weight.[30] While these studies used an

objective measure of sedentary time, the ability to determine the effect it may have on birth size is limited by the use of birth weight only (with no consideration of length and thinness). Further, the limited window of time in which sedentary behavior was measured during pregnancy does not capture the longitudinal or trimester-specific effects of this behavior. Thus, more research using objective measures of sedentary time across pregnancy, including weight-for-length or size for gestational age of the infant, are needed to ascertain the impact of sedentary behavior during pregnancy on fetal growth.

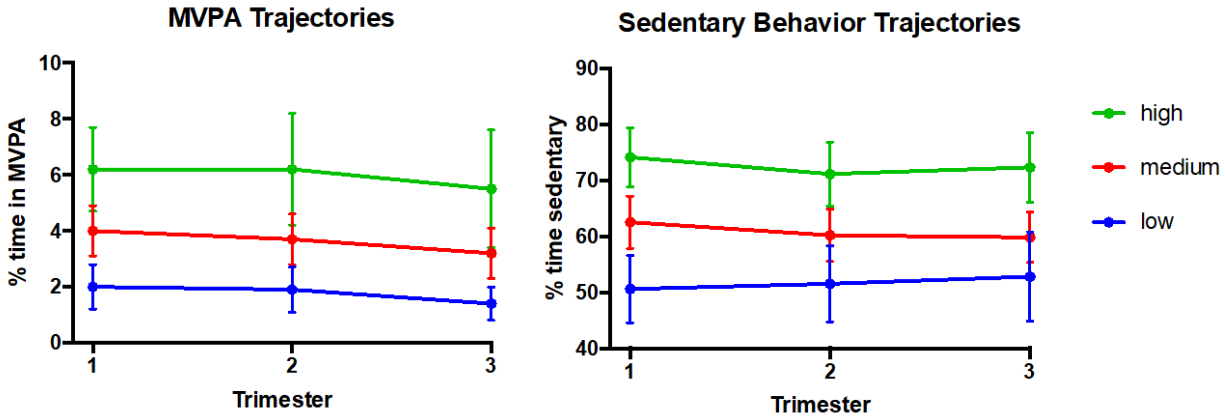

Figure 4. Maternal MVPA and Sedentary Behavior Trajectories

Preliminary data from our laboratory using objectively measured sedentary behavior in all three trimesters of pregnancy found that high sedentary time across pregnancy was related to lower ponderal index at birth, but not gross birth weight.[75] In this study, MVPA and sedentary behavior were objectively measured using a waist-worn Actigraph accelerometer and thigh-mounted activPAL accelerometer worn concurrently for one week in each trimester. Trajectories of both MVPA and sedentary behavior were generated and categorized women into high, medium, and low groups for each behavior (**Figure 4**).

Ponderal index of the offspring was calculated as birthweight (g) *100/ birth length $(m)^3$ based on weight and length measurements abstracted from medical records. Maternal MVPA trajectory was not significantly related to infant ponderal index at birth or birthweight, but being

in the highest maternal sedentary behavior trajectory was significantly associated with lower (worse) ponderal index of the infant ($p<0.001$). Moreover, sedentary behavior trajectory explained a substantial 13% of the variance observed in ponderal index. Associations of ponderal index by MVPA and sedentary behavior trajectory are displayed in **Figure 5**.

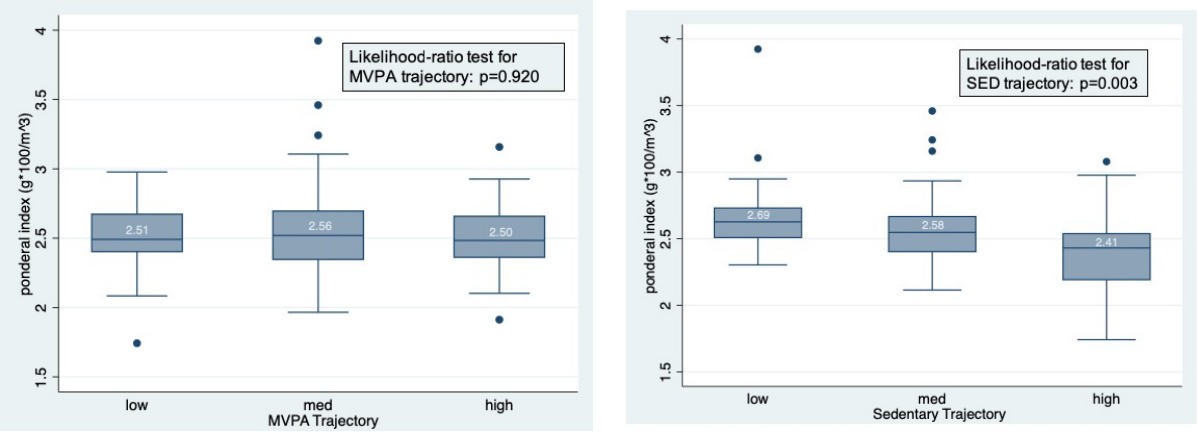

Figure 5. Ponderal Index by MVPA and Sedentary Behavior Trajectory Group

These findings are the first study to our knowledge to examine the association of prospective, gold-standard measurement of MVPA and sedentary time across pregnancy with birth size. The implications of high sedentary time on birth size could provide a modifiable behavioral intervention target that could potentially improve fetal development and subsequent lifespan health. Therefore, understanding the impact of sedentary time during pregnancy on early childhood health is an important research gap.

2.1.3 Maternal Activity Profile and Early Childhood Growth

The intrauterine environment and size at birth may have an effect a child's risk for catch-up or rapid growth.[33] As previously discussed, there is evidence to suggest that maternal MVPA and sedentary behavior may impact fetal growth *in utero,* however, whether these effects

persistently influence childhood growth rate is unclear. Previous studies have examined differences in childhood body mass between experimental and control groups following a maternal exercise intervention in pregnancy with mixed findings. One study including only previously active women compared a group of 20 women who maintained activity habits during pregnancy and another 20 who were instructed to stop physical activity in pregnancy. This study followed up on mothers and children at five years of age and found that children born to the mothers who maintained activity during pregnancy had lower body fat percentage versus those that discontinued exercise.[76] Contrasting these findings, a randomized controlled trial including a pregnancy exercise intervention (intervention: n=47, control: n=37) collected childhood anthropometrics at birth, one-year, and seven- years of follow up. Women in this intervention were previously inactive and exercised for 45-minutes x five times per week for 12 weeks in the second and third trimesters of pregnancy. This study found that women in the exercise intervention had children with a smaller birthweight compared to controls, but no differences in anthropometrics between groups were observed at one year. At seven years of follow-up, children from the exercise intervention actually had higher body fat percentage than the control group.[77] Lastly, a randomized control trial including dietary counseling and 30 to 60 minutes of unsupervised aerobic exercise per day in overweight or obese women assessed child anthropometrics between 2.5-3 years of age. This study included 77 intervention and 73 control participants and found no differences in BMI z-score's at follow-up assessments.[78]

Taken together, these studies provide conflicting results for the impact of prenatal exercise on early childhood growth rates. These differences in findings could be due to the differences in participant characteristics (i.e., previously active vs. inactive women, restriction to overweight or obese women), variable intervention dosage and timing, or the varying duration of follow-up for

measurement of anthropometrics in the children. These studies also only examined differences in body composition between experimental and control groups, rather than within-subject childhood growth patterns. More research is needed to clarify the effects of maternal MVPA on childhood growth rates.

In contrast, we are aware of no studies examining the associations of maternal sedentary behavior during pregnancy and rate of growth in childhood. Given our previous findings where high sedentary time was related to lower ponderal index, it is plausible that sedentary behavior may then relate to more rapid growth in childhood. Therefore, like for MVPA, the current evidence on maternal sedentary behavior in pregnancy is insufficient for determining the relationship with catch-up or rapid growth. The impact of maternal activity profile during pregnancy on early childhood growth rate is an important research gap.

2.1.4 Maternal Activity Profile and Motor Development

Motor skills development is foundational for children's physical, social, and psychological health.[79] Childhood development is typically measured with questionnaires or test batteries conducted by trained professionals. Examples of developmental test batteries include the Peabody Developmental Motor Scale (PDMS-2)[80] and Bayley's Scale of Infant Development.[81] Questionnaires measuring childhood development include Ages and Stages[82] (commonly used by physicians) and the Early Motor Questionnaire (EMQ).[83]

More recent studies have assessed motor, social, and neurodevelopment of children in relation to maternal MVPA. A meta-analysis of observational studies found that self-reported MVPA during pregnancy was associated with improved neurodevelopment, specifically general intelligence at age 5 and academic grades in school at age 10.[25] One randomized controlled trial

found that women in an exercise intervention (50 minutes of aerobic exercise, 3 times per week) had babies that scored higher on the locomotion component of the PDMS-2 at one month old.[84] The scores were higher in 4 out of 5 categories, but were only statistically significant for locomotion. Significant difference in other categories may not have been detected due to the small sample size of this study (n=27 control and n=33 intervention). Other categories that showed non-significantly higher scores among mothers randomized to the aerobic exercise group included stationary, gross motor quotient, and gross motor quotient percentile. On the contrary, other experimental evidence has found no significant associations between maternal MVPA and childhood development. One study (intervention n=164; control n=115) included a 3 day per week aerobic and strength training program and assessed children's motor development at 7 years of age. This study found no difference between intervention and control groups in fine motor, gross motor, language, behavioral, and perception scores based on the 'Five-to-Fifteen' questionnaire.[85] Another study with a similarly structured exercise intervention, though limited to aerobic exercise only (intervention: n=188, control n=148), measured children's development by Bayleys scale of Infant and Toddler Development at 18 months of age. This study also found no significant difference in motor, cognitive, language, or social development scores. However, motor development scores were nonsignificantly lower in the intervention group compared to control and, in sub-analyses by sex, motor development was significantly lower in boys.[86] Overall, maternal MVPA during pregnancy may have an effect on some domains of childhood development, though the direction of this effect and how long it persists in childhood remain unclear. There are still very few studies assessing the relationship between objectively-measured maternal activity and offspring motor, social, or neurodevelopment and none that evaluate the

effects of maternal sedentary behavior. Further, the wide variety of developmental measures make it difficult to compare current literature.

2.2 Short and Long-Term Offspring Health

As previously noted, Barker began the field of Developmental Origins of Health and Disease research with several cohort studies in England. He consistently found size at birth, including smaller birthweight, thinness, and SGA, to be associated with ischemic heart disease, insulin resistance, type 2 diabetes, coronary heart disease, and higher blood pressure in adulthood.[13-16,56] Beyond birth size, research also addresses rate of growth after birth which has been consistently associated with cardiometabolic health across the lifespan. Specifically, more rapid growth, especially when accompanied by small birth size, is associated with poorer cardiometabolic health long-term.[45,87] This rapid growth is commonly called catch-up growth and infants born with lower birth weight, lower ponderal index, or SGA are at a greater risk. This is thought to be a result of the 'mismatch' theory described in section 2.1 in which the environment after birth is more nutrient rich than the *in utero* environment.[66] The short- and long-term impact of birth size or catch-up growth on many domains of health have been extensively studied within the Developmental Origins of Health and Disease theory and are discussed in detail in the following sections.

2.2.1 Cardiovascular Health

Associations of birth size with cardiovascular diseases have been conducted across the lifespan and have assessed subclinical and overt disease outcomes. In one meta-analysis of the incidence of ischemic heart disease, the hazard ratio for ischemic heart disease decreased by 10-20% for every 1 kg increase of birthweight.[88] This meta-analysis included follow-up from 17 longitudinal studies.

Perhaps one of the most common measures of cardiovascular health is blood pressure, which is a major risk factor for cardiovascular disease and mortality.[89] Elevated blood pressure detected in children is a marker of poor cardiovascular health in early life and a risk factor for cardiovascular disease later in life.[90] In one cohort study of 346 individuals, blood pressure at 22 years was inversely associated with birthweight. Systolic blood pressure was higher by 1.3 mmHg for every z-score decrease in birth weight and was 1.6 mmHg higher for every z-score increase in childhood weight gain. In this study, the effect on blood pressure was greater if an infant born small also had rapid growth. Of note, rapid growth was not independently associated with higher blood pressure without also considering the presence of small birth size.[91] In a systematic review of prospective cohort studies ranging from childhood to older adults, birthweight was inversely associated with systolic blood pressure. This relationship was weak in adolescence but strengthened with age thereafter.[92] In another study, a cohort of 145 individuals found that birth weight and current body mass index (BMI) were associated with 24-hour blood pressure at 5 years old.[9] Again, in a study of 395 eight-year-olds, birthweight and rapid weight gain were associated with higher blood pressure and greater carotid intima thickness (a marker of arterial health).[93] Thus, consistent evidence supports a link between small birth size, rapid growth during early childhood, and lifetime risk for hypertension.

Heart rate variability is another subclinical marker of cardiovascular disease that measures autonomic function by sympathetic and parasympathetic control.[94] This has been measured in infants as a subclinical indicator of cardiovascular system regulation. Among 200 newborns, both high and low body fat percentage at birth was associated with lower (worse) heart rate variability. Fat percentage accounted for 8.7% of the variance in overall heart rate variability, suggesting that adiposity is a significant driver of autonomic function.[95] In another study of 27 infants, heart rate variability was lower (worse) at one and three months follow-up in SGA babies compared to babies with adequate weight for gestational age.[96] Evidence of longer term effects of birth size on heart rate variability and autonomic function disturbance does not exist and is thus an area for future research.

Taken together, these studies suggest that smaller size at birth, particularly when paired with rapid growth in childhood, is associated with poorer cardiovascular health. This consistent finding is observed across subclinical cardiovascular health markers in childhood and further manifests as higher cardiovascular disease risk in adulthood.

2.2.2 Metabolic Health

Risk for type 2 diabetes has also been consistently associated with smaller birth size. Thus, associations between birth size and several measures of metabolic function across the lifespan have been studied. In the Helsinki birth cohort of 474 participants, ponderal index, birth weight, and rapid childhood growth were inversely related to 2-hour fasting insulin at approximately 64 years old.[12] More recently, a meta-analysis found that continuous birthweight was inversely associated with risk for type 2 diabetes later in life. This association weakened with age of follow-up but remained significant with adjustment for current body size.[47] This meta-analysis only included

diagnosed cases of type 2 diabetes and did not use studies measuring continuous insulin levels only. Homeostatic model assessment (HOMA) index is also used as a marker of metabolic function as a ratio of insulin to glucose in the blood. In a cohort study, babies born SGA had higher HOMA index at 5 and 10 years old. Also in this study, SGA babies had the lowest HDL and highest fasting insulin, indicating overall metabolic dysfunction.[8,9] Therefore, smaller size at birth is a risk factor for future type 2 diabetes and poorer metabolic function across the lifespan.

2.2.3 Adiposity and Body Size

Several studies have found adverse associations between birth size, catch-up growth, and body size or composition later in life. In a cohort study of 850 participants, lower ponderal index, lower birth weight, and catch-up growth in the first year were associated with greater waist circumference, BMI, and fat mass percentage at 5 years old.[10] This association persisted after adjustment for infant feeding type. A similar relationship was found to continue across the lifespan in the Helsinki birth cohort which found higher waist circumference at 64 years old in those born smaller or thinner.[12] One important factor to consider is that these studies are inclusive of low and very low birth weight infants (<2,500 g). Due to the elevated risk of infant morbidity and mortality associated with low birth weight,[97] including these births could partially explain the observed associations.

However, poorer adiposity outcomes are also observed in individuals considered adequate for gestational age at birth but with signs of growth restriction. Those babies born adequate for gestational age with growth restriction had a lower ponderal index, head circumference, and less lean mass than those born adequate for gestational age without growth restriction.[48] Additionally, the growth restricted infants with adequate weight for gestational age had overall similar metabolic

profile to SGA babies, rather than non-growth restricted adequate for gestational age infants.[48] Another cohort study assessing growth in adequate-weight-for-gestational-age infants compared birth characteristics of children who had rapid growth vs non-rapid growth in the first year of life. This study found that rapid growers were smaller at birth by birthweight and had higher body fat percentage and BMI at 7 years old.[11]

Infants born with adequate birthweight still have a higher risk for greater adiposity in childhood and adulthood if growth restriction occurred *in utero*. Whether prevention of growth restriction by improving the intrauterine environment could reduce the risk for overweight or obesity remains unknown.

2.2.4 Childhood Motor Development

Very little is known about how fetal growth may affect developmental milestones in childhood. Development is an important measure as poorer or delayed motor development is related to increased risk for obesity and lower levels of MVPA[36,37] in childhood. There is only one relevant available study to our knowledge which assessed over 4,000 infants in NHANES (1988-1994). This study found that term (≥37 weeks gestation), low birth weight infants and preterm (<37 weeks gestation), low birthweight infants both had lower motor-social development scores between 2-47 months of age when compared to infants with normal birth weight. In females, low birthweight was the most important prenatal predictor of delayed social motor development.[98] Motor skills development is positively associated with cardiorespiratory fitness and inversely related to risk of obesity in childhood.[99] A better understanding of how fetal growth relates to early childhood motor skills development is needed to identify children at potential risk and prevent the occurrence of developmental delay.

2.2.5 Implications of Large Birth Size

It is a commonly thought that there is a U-shaped association between birth size and all of the previously noted health risks. In other words, in addition to low birth weight, poor health outcome such as obesity, type 2 diabetes, and cardiovascular disease in adulthood are also thought to be related to high birth weight. However, based on the evidence, most childhood and adult cardiometabolic outcomes are only associated with SGA, lower birthweight, or lower weight-for-length. LGA appears be a risk factor for the development of only certain diseases in the offspring but mostly when it occurs in the context of GDM.

A large Swedish birth cohort of over 700,000 individuals found that hazard ratios for type 2 diabetes increased by birthweight category.[100] However, this study did not take into account maternal GDM as testing is not standard in Sweden. This is an important consideration as the long-term risks associated with LGA are most prevalent when the pregnancy is complicated by GDM. LGA infants born to women with GDM had a higher prevalence of metabolic syndrome at 6, 7, and 11 years old as compared to LGA infants without GDM or adequate-for-gestational age infants with or without GDM.[101] In a systematic review of the literature, high birth weight (>4000 grams), especially when accompanied by poorer maternal glycemia, was associated with an increased risk for obesity. In the same study, high birth weight was not associated with the risk of coronary heart disease or hypertension.[102]

In terms of development, in a cohort study of 4,000 individuals, LGA newborns actually had better developmental learning skills between 7-9 years of age.[103] This was based on the Australian Early Development Census which includes general knowledge, cognitive function, emotional maturity and skills function.

Overall, relationships between birth weight and long-term outcomes are complex. LGA or high birthweight should be a concern for future obesity risk when accompanied by GDM, but LGA does not appear to elevate risk for other cardiometabolic domains and might even be beneficial for development.

2.3 Physiological Mechanisms

Physiological mechanisms explaining the Developmental Origins of Health and Disease hypothesis have been a focus of more recent research. While much of the physiological processes underlying the programming of disease risk remains unknown, there are proposed mechanisms including placental alterations and structural changes of the developing fetus. Though we do not plan to measure these specifically in the proposed study, we discuss them below to demonstrate the biological plausibility of our hypotheses that maternal activity profile could affect early childhood growth and development.

2.3.1 Placental

The placenta is thought to be at the forefront of fetal programming as it is the link between maternal health and the developing fetus. A review of chronic disease programming research concluded that much of the risk for chronic diseases can be linked to characteristics of the placenta.[104] Supporting this idea is one observational study of 206 individuals that found lower ponderal index was related to the oxygen tension of the placenta.[105] Oxygen tension is a measure of blood flow and sufficiency of nutrient delivery from the placenta. These findings support the

hypothesis that growth restricted fetuses may be a result of reduced blood flow and nutrients, but it does not explain what led to the insufficient placenta. Another study assessing physical activity during pregnancy found that a higher amount of objectively measured MVPA was related to increased capacity for nutrient transport across the placenta via gene expression.[19] This data points to physical activity as a potential mechanism to improve placental sufficiency. The implications of reduced blood flow and oxygenation to the fetus provides one mechanistic explanation for the Developmental Origins of Health and Disease.

2.3.2 Structural: Animal Studies

The basis of much of the Developmental Origins of Health and Disease hypothesis was predicated on animal models. Animal models have demonstrated permanent structural variation in organ systems and hormone regulation with prenatal dietary modification or induced growth restriction. One study in sheep found that, when intrauterine growth restriction was induced, placental insufficiency occurred. Further, the carotid and umbilical arteries had higher collagen and lower elastin levels.[42] This demonstrates an increase in arterial stiffness in offspring that have experienced growth restriction. Further animal studies using dietary modification to replicate fetal undernutrition in humans found that mice with low-energy, low-protein diets had offspring with less functional pancreatic cells than those with adequate diet.[40] Less pancreatic cells can reflect a decreased ability to regulate insulin and glucose.[106] Effects on the kidney have also been found in other animal studies. One study found that protein deficient rats had offspring with less nephrons and suppressed renin-angiotensin aldosterone system (RAAS) function.[41] Functional nephrons and the RAAS are partly responsible for blood pressure regulation,[107] suggesting a mechanism for lifetime impairment in vascular health among these offspring. If these animal models reflect what

occurs in humans, these studies could begin to explain the link between undernutrition and smaller birth weight with hypertension, reduced insulin function, and diabetes later in life.

2.3.3 Structural: Human Studies

We are aware of only one human study that has been conducted to assess differences in organ system development in the context of intrauterine growth restriction. This study assessed the relationship of birthweight to cardiac structure in childhood and found that, independent of current height and weight, birthweight was inversely associated with coronary artery diameter at 9 years old. The authors noted that smaller coronary artery diameter is associated with higher prevalence of atherosclerotic lesions.[44] This may explain another mechanism by which lower birthweight is associated with long-term cardiovascular disease. However, more research is needed to elucidate the biological cascade that relates maternal undernutrition and other sources of intrauterine growth restriction to long-term impairments in offspring vascular and metabolic health.

2.4 Role of Social Determinants in Developmental Origins of Health and Disease

It is important to acknowledge that the interaction of many factors is likely responsible for fetal programming and the Developmental Origins of Health and Disease. There are a number of modifiable and non-modifiable factors that affect health in general. Social determinants of health are the conditions in which individuals live, work, and interact including socioeconomic status, education, employment, and access to health care.[108] These factors impact health for a multitude

of reasons including access to transportation, quality of care, and literacy, as well as chronic stress and discrimination.[108] Therefore, the following section will consider various social determinants of health and their potential implications on fetal programming.

Only one study explicitly examined the Developmental Origins of Health and Disease in regard to socioeconomic status. This study found that, in the Helsinki birth cohort, the hazard ratio for coronary heart disease increased as income decreased. However, low ponderal index at birth exacerbated this effect while those born with normal fetal growth were more resilient to the health effects of living in poverty.[109]

While not explicitly studied in the context of fetal programming, it does appear that race/ethnicity and socioeconomic status impact birth size, fetal growth, and risk for pregnancy complications, all factors associated with long-term health of offspring. A cohort study of 2,103 individuals in Quebec, Canada found that maternal education and family socioeconomic status were directly associated with birthweight. Single-parenting and smoking were inversely related.[110] This study suggests that individuals with lower income and lower education have a higher risk of having a smaller baby, which would then be thought to increase the risk for future disease.

Birth size by racial and ethnic groups has been fairly well studied in prospective cohort studies. The National Institute of Child Health and Human Development fetal growth cohort of 1,737 fetal-mother pairs found that babies born to White women had the highest mean birthweight followed by Hispanic, Asian, then Black.[111] One large study of >220,000 participants in a multi-ethnic cohort found variations in the risk of LGA birth by race and ethnicity. More specifically, this study assessed 1) GDM, 2) pre-pregnancy adiposity, and 3) excessive gestational weight gain as three risk factors for LGA birth and how the presence of multiple factors compounds the risk for a large infant. They found that the odds for LGA doubled when all 3 factors when present in

whites and Hispanics but not in Asians. Further, GDM alone did not increase risk for LGA infant in White non-Hispanics, but greatly increased risk in all other races. Finally, in all categories from 1,2, and 3 risk factors, Black individuals had the highest risk for LGA when combined with GDM.[112]

Growth and risk for obesity also have shown racial/ethnic differences. Hispanic and Black children had the sharpest increase in BMI by 4 years old, most prominently in Hispanics living in Spanish-speaking homes. Among these individuals, forced feeding and early or no breastfeeding was more common compared to White individuals.[113] This is supported in another study of 1,800 infants which found that rapid infant weight gain to 6 months, restrictive feeding of mother in pregnancy, and lower breastfeeding were all more common in Black and Hispanic mothers than White mothers.[114] Within this same cohort, Black and Hispanic infants had an increased odds of obesity at 3 years which was associated with lower birthweight and gestational age. These babies were born smaller and grew faster in the first six months than White babies.[114]

Further, common determinants of birthweight include excessive gestational weight gain, GDM, smoking, and feeding type. When compared across race groups, Black and Hispanic women had higher rates of GDM but lower rates of excessive weight gain and smoking than White women. Rapid weight gain, early solid food introduction, and less breastfeeding was also more common in Hispanic and Blacks. Seven-year follow up in this cohort found higher body fat percentage, higher BMI z-score and higher percentage of overweight and obesity in Hispanic and Black children compared to White; this relationship was attenuated after statistical adjustment for birthweight and gestational weight gain.[115]

Lastly, in addition to differences in birth outcomes and childhood growth, type of or perceptions of physical activity during pregnancy may differ by sociodemographic factors. One study found that Black women were less likely to express intention to meet exercise recommendations in pregnancy compared to White women.[116] White race, higher education, or having no other children in the home is consistently related to higher activity levels during pregnancy.[117] Further, occupational activity (as opposed to leisure time physical activity) is more common in lower income, minoritized groups.[118,119] Higher levels of occupational activity has been related to a greater risk for adverse pregnancy outcomes[120] as opposed to leisure time physical activity which is related to a lower risk of adverse pregnancy outcomes.[121,122] This suggests that type of physical activity may have differential effects on the fetal environment.

Taken together, these data suggest that upstream factors (displayed in **Figure 1**) affect maternal behaviors and play a role in the Developmental Origins of Health and Disease. Further, the effects of maternal factors on the intrauterine environment may not affect all individuals equally. Considering socioeconomic status, race, ethnicity, and education is important to fully understand health and disease risk across the life span.

2.5 Conclusion

There is strong evidence to support Developmental Origins of Health and Disease and that the fetal environment is a reflection of maternal health and behavior that could program long-term health in the offspring. Understanding that MVPA and sedentary behavior impact birth size and the fetal environment offers a novel, modifiable behavior in pregnancy to potentially improve fetal growth. This is of great importance due to the impact that fetal growth has on health and disease

susceptibility across the lifespan. Rate of growth and motor development in early childhood are important indicators of future health. However, the effect of MVPA and sedentary behavior on these outcomes remain unknown. This knowledge could inform the basis for MVPA or sedentary behavior interventions and recommendations during pregnancy. These interventions could potentially affect the health of future generations and are therefore an important and critical contribution to improving population health.

3.0 Methods

3.1 Study Design

The present study is a follow-up on participants enrolled in the MOnitoring Movement and Health (MoM Health) study (conducted March 2017- April 2019). MoM Health was a prospective cohort study assessing activity profile across pregnancy, including objectively-measured sedentary behavior and MVPA, as well as maternal health and infant outcomes at birth. This dissertation project, the MoM Health 2.0 study, examined associations between maternal activity profile during pregnancy with childhood growth pattern and motor development in early childhood. Within the parent study, women attended three study visits, one in each trimester of pregnancy. Participants wore two activity monitors at each study visit to monitor activity profile for one week. The MoM Health 2.0 study collected additional data (from February 2020 – June 2020) via survey and medical record abstraction on the growth and development of the child born during the pregnancy monitored in the MoM Health study with the following Aims:

Specific Aim 1: To examine associations between maternal activity profile across pregnancy and by trimester with infant growth rate up to 24-months of life.

Hypothesis: Higher maternal sedentary behavior and lower maternal MVPA will be related to greater risk of catch-up growth and more rapid growth rate.

Specific Aim 2: To examine associations between maternal activity profile across pregnancy and by trimester with child motor development.

Hypothesis: Lower maternal sedentary behavior and higher maternal MVPA will be related to more advanced motor development.

Exploratory Aim: To evaluate the influence of BMI z-score at birth on associations observed in Aims 1 and 2.

Hypothesis: Covariate adjustment for BMI z-score will attenuate the associations between maternal activity profile and early childhood growth and motor development.

3.2 Sample Population

Mother-child dyads were recruited for the present study from participants who completed the MoM Health (parent) study. Pregnant women were recruited for the parent study in the following ways: 1) flyers placed at obstetrics and gynecology practices, 2) University of Pittsburgh Clinical and Translational Science Institute research registry, 3) emails to University of Pittsburgh employees, and 4) referrals from other research studies or word of mouth. Women were eligible for the parent study if they were between the ages of 18-45, <14 weeks pregnant, not taking any hypertensive or diabetes medications, and able to walk a half of a mile and climb two flights of stairs. Inclusion and exclusion criteria for MoM Health 2.0 study can be found in **Table 1.**

Table 1 Study Inclusion and Exclusion Criteria

Inclusion Criteria
• Child was born to the mother during her participation in the MoM Health study
• Child is ≥12 months old
• Born from a singleton pregnancy
• Mother has ≥1 trimester of valid objective activity monitoring available through the MoM Health study
Exclusion Criteria
• Presence of any chromosomal or congenital abnormalities of the child that may affect growth or development
• Mother does not have custody of child

Participants from the parent study with ≥1 trimester of valid objective activity monitoring and a singleton live birth (n=103) were deemed initially eligible for recruitment contact and additional screening. Recruitment efforts for the current study included an email containing an informational flyer (**Appendix A**) sent to all eligible participants, followed by a minimum of two subsequent contacts (phone or email) made to non-responders. Interested participants were sent a link to an online screening and e-consent form. The screening form (**Appendix B**) further assessed inclusion and exclusion criteria by self-report. Prospective participants were able to review the e-consent document on their own and were able to sign using a mouse or stylus to draw in their signature. Eligibility criteria had to be met on the screening form and e-consent signature was required prior to moving forward to the surveys.

3.3 Assessment Procedures

Upon completion of the online e-consent form, enrolled mothers completed an electronic questionnaire battery about their child's motor development, as well as important covariates including demographics and infant feeding type. Access to medical records from their child's pediatric visits since birth were obtained through the consent process. Surveys were reviewed for completeness and, in the case of illogical or incomplete answers, mothers were contacted for clarification. Screening, e-consent, and questionnaire data collection processes were all conducted using the REDCap (Research Electronic Data Capture) web-based software platform. [123] [123] [122] [121] [121] [120] [119] [118] [117] [116] [116] [116]

Mothers consented to share medical records from their child's pediatric visits since birth. Medical records not available through the University of Pittsburgh Medical Center electronic health record were requested using clinic-specific medical record request forms signed by the mother. Medical record data were abstracted independently by the principal investigator and a trained research staff member. Records were assessed for differences and adjudicated with consensus.

Participants were compensated using the University of Pittsburgh's 'man on the street' Vincent payment system for completion of the survey and provision of consent to access medical records. Participants had the option to receive $20 by loading funds onto an existing Vincent payment card or as a virtual Target or Amazon gift card.

3.3.1 Maternal Activity During Pregnancy

Maternal activity profile data were previously collected during the MoM Health study. Data were collected during each trimester using gold standard, objective assessment methodology. MVPA was measured by a waist-worn Actigraph GT3X accelerometer (Actigraph, Pensacola, FL). Participants were instructed to wear the Actigraph on the right hip during all waking hours, only to be removed for sleep or water activities (bathing or swimming). Sedentary behavior was measured using a thigh-mounted activPAL accelerometer (PALtechnologies, Glasgow, Scotland) following a 24-hour wear protocol, only to be removed for swimming. Participants were instructed to wear monitors concurrently for 7 days, and data were considered valid if worn for $\geq$10 hours on $\geq$4 days. Percentage of monitor wear time spent in sedentary behavior and MVPA were considered in analyses. Data were processed using standard methodology.[124,125]

Trajectories across pregnancy were generated separately for MVPA and sedentary behavior using growth mixture modelling analysis.[126] Best fit for trajectory groups were selected based on the Bayesian criterion index (BIC), greatest percentage of participants placed in groups with posterior probability of $\geq$ 70%, and clinical relevance. Women were assigned to one of 3 trajectories groups (high, medium, and low) for each sedentary behavior and MVPA. Specific details and figures displaying these trajectories can be found in Chapter 2, section 2.2.1. These sedentary behavior and MVPA trajectories, along with continuous trimester-specific sedentary behavior and MVPA of the mother, are considered the independent variable in the present study.

3.3.2 Infant Birth Size and Growth Pattern

All available height/length and weight measures were abstracted from child medical records from birth to 24 months of age. Anthropometric measures from each visit were converted into age-specific body mass index (BMI) z-scores using the STATA World Health Organization z-score calculator plug-in.[127] Growth pattern was assessed using two definitions: catch-up growth (primary approach) and growth rate (secondary approach). Catch-up growth was operationalized as a dichotomous variable defined as an increase in z-score from birth to one year of age $\geq$2.0.[128] Growth rate was examined using incremental rate of BMI z-score change estimated by a line of best fit using all available BMI z-scores between birth and 24 months from medical records.

3.3.3 Questionnaires

Mother participants completed a battery of questionnaires via REDCap online survey system. Demographic and health-related information was collected using the questionnaire found in Appendix C.

Retrospective self-reported infant feeding behaviors were collected using a modified breastfeeding survey (Appendix D). Mothers reported if they breastfed or provided pumped breastmilk to their child and, if so, for how long. Exclusivity of breastfeeding along with introduction of formula and solid foods was collected. Information regarding feeding habits was abstracted from medical records and used to corroborate self-report.

The parent-reported Early Motor Questionnaire (EMQ)[83] was used to measure motor development (Appendix E). Participants responded to questions using a 5-point scale ranging from -2 (sure child does not show behavior) to +2 (sure child shows behavior). The questions provide a

composite score in three domains: gross motor (GM), fine motor (FM), and perception-action (PA). The three domain scores correspond to full body movements and large muscle group control (gross motor), small muscle groups and ability to grasp, hold, or manipulate objects (fine motor), and a child's ability to use their senses to gather information and respond to the world around them (perception action).[129] An instructional video accompanied the questionnaire to aid in proper completion of the EMQ. The EMQ is widely used to measure parent-reported motor development in children aged up to 24 months and has high concurrent validity with gold standard examiner-administered motor development measure (GM: $r = .97$, FM: $r = .91$, PA: $r = .91$).[83] EMQ scores are expected to increase with age and plateau at approximately 24 months. Due to wide variations in age within our sample, including n=26 children >24 months of age, two methods were employed to account for age differences across participants: i) age-adjusted models (primary approach) and ii) age-standardization of EMQ scores (secondary approach). Age-adjusted models used raw EMQ scores as the dependent variable with adjustment for age using a linear spline with an inflection point at 24 months. This methodological choice reflects that the EMQ score is expected to increase more steeply up to age 24 months and then be more stable after 24 months. Age-standardization analyses generated scores using quadratic standardization equations provided by Dr. Libertus from 750 children with varying ages. Since these standardization equations were calculated using few children above 24 months old and we had a meaningful proportion of participants above 24 months old, these standardized scores were used as a secondary analysis approach for comparative purposes.

Mothers were asked to recall the age that their child first started to crawl and walk and report on what records, if any, were used to estimate the age of onset for these behaviors. Recall

options included their own diary, photo, or video records (e.g., Facebook or pictures on a cell phone) or subjective recall from memory. This questionnaire can be found in Appendix F.

3.4 Power Considerations

A first consideration is that we were limited by the sample size from the parent study (n=103). Though we hoped to obtain medical records for ~80% of our sample, we had a lower response rate of 70% (see Results). As no previous studies provide expected effect sizes for our outcomes, post-hoc power analyses were conducted. Catch-up growth analyses was possible for n=60 participants with complete data. Assuming an even distribution of the rate of catch-up growth across trajectory groups, and a 20% prevalence of catch-up in the unexposed (reference) group, we would have had 80% power to detect an OR of 7.8 with a significance level of 0.05. In motor development models, based on our data with n=70, age splines explained roughly 45% of the variance. Activity trajectory would have had to explain an additional 7% of the variance to have 80% power at an alpha level of 0.05.

Therefore, the present study may be limited in power to detect significant associations with outcomes due to these limitations and is thus exploratory and hypothesis-generating in nature. Smaller and/or non-significant effects in these data still provide power and sample size estimates for future studies.

3.5 Statistical Analysis

Statistical analyses were performed using Stata 14 software (StataCorp, College Station, TX). Descriptive statistics described the characteristics of the sample including maternal and child demographics, feeding type, and age at questionnaire completion. Specific Aims 1 and 2 were assessed using two approaches to operationalize the independent variable: the primary approach used categorical maternal sedentary behavior and MVPA trajectory groups (described in Chapter 2, Section 2.1.1.), and the secondary approach constructed separate models by trimester with continuous maternal sedentary behavior and MVPA. In models including continuous sedentary behavior or MVPA by trimester, all beta coefficients and odds ratios were standardized to the independent variable to facilitate comparison of results.

To evaluate Specific Aim 1, logistic regression models examined the odds of dichotomous catch-up growth occurring by maternal sedentary behavior and MVPA. Mixed linear regression models examined the relationships between maternal sedentary behavior and MVPA (independent variables) with growth rate as measured by incremental rate of BMI z-score change (dependent variable).

To evaluate Specific Aim 2, linear regression models using age-adjustment (primary) and age-standardized scores (secondary) examined the relationship between maternal sedentary behavior and MVPA and the three EMQ score domains. Semipartial correlations were used to assess the effect size (meaningfulness) of associations in which <0.2 is considered weak, 0.2-0.5 moderate, and >0.5 strong effect.[130] Associations of maternal sedentary behavior and MVPA with crawling and walking onset age were examined using linear regression models. Predicted least square mean EMQ scores as well as crawling and walking onset age were used to illustrate averages by maternal activity trajectories.

To evaluate our exploratory aim, models examining attenuation of the relationship between maternal sedentary behavior and MVPA with catch-up growth and EMQ scores were assessed by examining associations before and after inclusion of BMI z-score at birth as a covariate. Similar analyses testing attenuation of the relationship between maternal sedentary behavior and MVPA and the incremental change in BMI z-score were not possible because BMI z-score at birth was already included in the model. Changes in magnitude and significance of associations were qualitatively assessed in each model with and without adjustment for BMI z-score at birth to explore the potential for mediation (attenuation).

With considerations for parsimony given our limited sample size based on the parent study and survey response rates, associations of participant characteristics that could potentially confound our analyses were evaluated for all outcome measures in secondary analyses. These sensitivity analyses were conducted whereby the potentially confounding characteristics were tested for influence on the relationship of interest one at a time in each statistical model (Aims 1 and 2).

4.0 Results

The purpose of this prospective cohort study was to evaluate the associations of maternal sedentary behavior and MVPA during pregnancy on early childhood growth and motor development. The results are presented below beginning with description of study participants and following with results organized by specific aims.

4.1 Study Participants

4.1.1 Recruitment and Enrollment

A flow diagram describing participants included in the current study is presented in **Figure 6.** A total of 103 women who previously participated in the MoM Health study were contacted for participation in this study. Recruitment approach included a minimum of three contacts (initial email, then up to two emails/phone calls) to each potentially eligible participant. Of those contacted, n=25 did not respond, and n=78 responded and expressed interest in participating. The 78 responders were sent consent and screening forms. Of these, n=4 did not consent or respond to follow-up contacts and n=74 consented and were deemed eligible based on screening criteria. Four enrolled participants completed the consent and screening but did not complete any study questionnaires (n=2) or did not complete the Early Motor Questionnaire only (n=2), resulting in 72 participants with complete or partially complete questionnaire data. Medical records were available through University of Pittsburgh Medical Center for 50 participants. Medical records

requests were signed and submitted to pediatric clinics for 20 participants. Of these, 12 were processed and received, resulting in 62 medical records available.

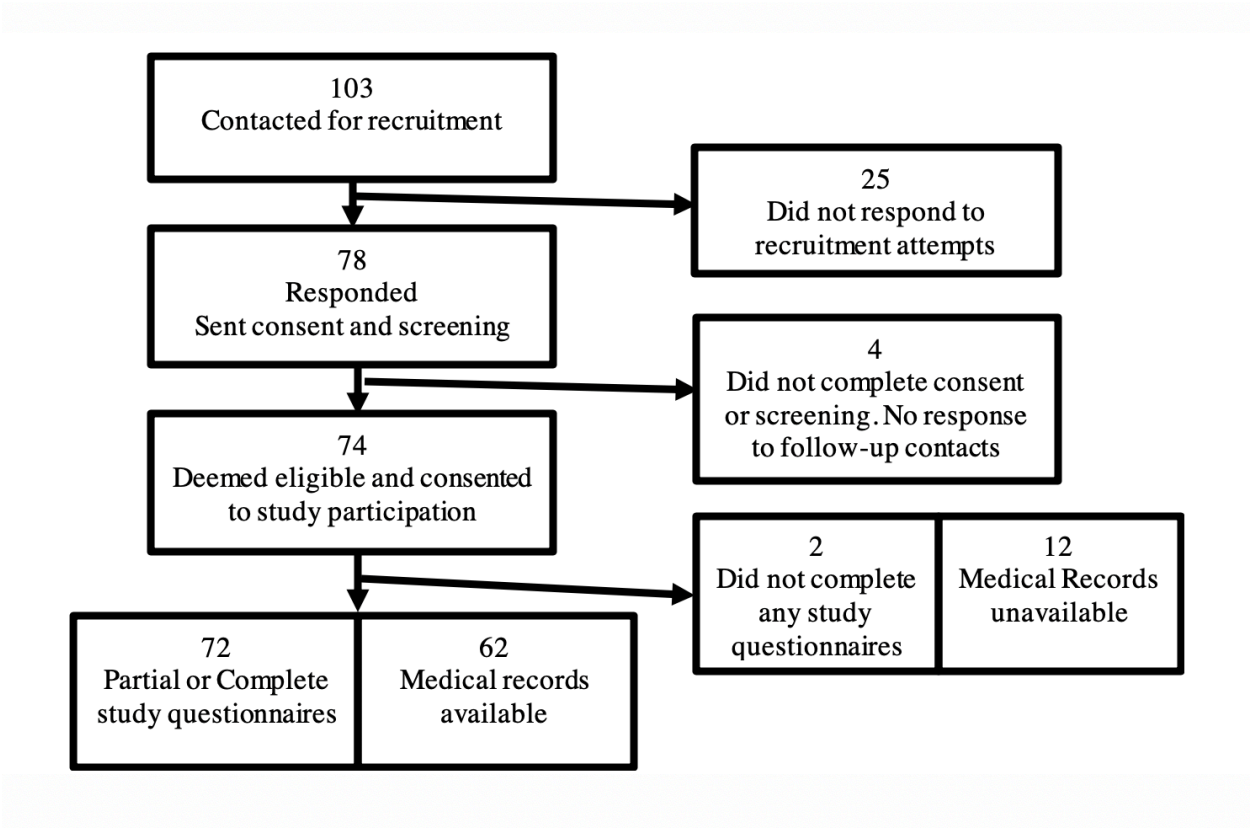

Figure 6 Diagram of Participant Enrollment in the MoM Health 2.0 Study

4.1.2 Participant Characteristics

Seventy-two mother-child dyads were included in this study. Children were between the ages of 13-30 months old at time of data collection with a mean (SD) age of 21.8 (5.2) months. Children in this study sample were 53% male, primarily white (84%), and had mothers who were highly educated (58% had a masters or doctoral degree). Demographic and clinical characteristics

are summarized in **Table 2** overall and by maternal sedentary and MVPA trajectory. No characteristics significantly differed across activity trajectory groups.

Table 2. Maternal and Child Characteristics Overall and by Activity Trajectories

		Sedentary Trajectory (n)				MVPA Trajectory (n)			
Mean (SD)	Overall (72)	Low (13)	Med (30)	High (29)	p-value	Low (18)	Med (39)	High (15)	p-value
Child age, months	21.8 (5.2)	23.7 (5.4)	21.3 (5.3)	21.4 (5.1)	0.353	21.8 (5.9)	21.7 (5.0)	22.1 (5.3)	0.967
Gestational age at birth, weeks	39.1 (1.5)	39.4 (0.9)	39.0 (1.3)	39.0 (1.9)	0.702	39.2 (0.8)	39.2 (1.7)	38.6 (1.6)	0.357
Maternal pre-pregnancy BMI, kg/m^2	26.1 (6.8)	29.5 (8.6)	24.9 (5.6)	25.9 (6.7)	0.117	27.2 (8.0)	25.6 (5.2)	26.3 (8.8)	0.704
Maternal EPDS score*	3.3 (3.2)	3.8 (3.7)	2.4 (2.7)	4.0 (3.3)	0.224	3.7 (2.4)	3.0 (3.2)	3.5 (4.3)	0.781
n (%)									
Sex					0.079				0.337
Male	38 (53)	5 (38)	13 (43)	20 (69)		12 (66)	18 (46)	8 (53)	
Female	34 (47)	8 (62)	17 (57)	9 (31)		6 (33)	21 (54)	7 (47)	
Feeding type					1.00				0.780
Exclusively breastfed	36 (50)	7 (54)	15 (50)	14 (48)		9 (50)	20 (51)	7 (47)	
Partial breastfeeding	33 (46)	6 (46)	13 (43)	14 (48)		9 (50)	16 (41)	8 (53)	
Exclusively formula fed	3 (4)	0	2 (7)	1 (4)		0	3 (8)	0	
Maternal Education					0.264				0.130
Highschool or less	1 (1)	0	0	1 (2)		1 (5)	0	0	
Some college or training	11 (15)	4 (31)	4 (13)	3 (10)		5 (28)	3 (8)	3 (12)	
College grad	18 (25)	4 (31)	5 (17)	9 (31)		5 (28)	11 (28)	2 (12)	
Masters/Doctoral	42 (58)	5 (39)	21 (70)	16 (55)		7 (39)	25 (64)	10 (67)	
Household Income					0.270				0.436
<50,000	6 (8)	3 (23)	2 (7)	1 (3)		1 (6)	4 (10)	1 (7)	
50-<75,000	8 (11)	2 (15)	4 (13)	2 (7)		3 (17)	4 (10)	1 (7)	
>75,000	55 (76)	7 (54)	23 (77)	25 (86)		12 (67)	31 (79)	12 (80)	
Don't know/refused to answer	3 (4)	1 (8)	1 (3)	1 (4)		2 (11)	0	1 (7)	
Race					0.852				0.531
White	60 (84)	10 (77)	26 (86)	24 (83)		13 (72)	33 (84)	14 (93)	
Black	6 (8)	2 (15)	2 (7)	2 (7)		2 (11)	3 (8)	1 (7)	
Other	6 (8)	1 (8)	2 (7)	3 (10)		3 (17)	3 (8)	0	

EPDS: Edinburgh Postpartum Depression Score, BMI: Body Mass Index

*Fewer observations available for EPDS score (n=49)

A comparison of characteristics between the parent study sample and responders to this follow-up study is presented in **Supplemental Table 1** in Appendix G. Distribution across maternal sedentary and MVPA trajectories did not differ between samples. Further detail regarding maternal sedentary behavior and MVPA from the parent study is presented in Figure 2 in Chapter 2, Section 2.1.1. Women that responded and enrolled in the present study were significantly younger, more highly educated, and less racially diverse than the parent study sample.

4.2 Specific Aim 1

The first aim of this study was to examine how maternal activity profile during pregnancy relates to infant growth (BMI z-scores) during early childhood. Growth rate was operationalized using a primary (catch-up growth) and secondary (growth rate) method.

4.2.1 Catch-up Growth

BMI z-scores at birth and 12 months were available for n=60 participants. Mean (SD) BMI z-score was -0.69 (1.17) at birth and 0.03 (0.97) SD at 12 months, with an average change of 0.70 (1.41) between birth and 12 months. Catch-up growth, operationalized as an increase in BMI z-score $\geq$2.0 between birth and 12 months, occurred in n=14 (23%) of participants. A comparison of participant characteristics between those with and without catch-up growth can be found in **Supplemental Table 2** in Appendix G. Gestational age at delivery was the only characteristic that significantly differed across groups, with a lower mean gestational age (37.9 [2.0] weeks) in those that experienced catch-up growth than in those that did not (39.3 [1.3] weeks). Of note, while not statistically significant, all cases of catch-up growth occurred in White participants and other characteristics such as maternal education and prepregnancy BMI differed meaningfully.

Unadjusted logistic regression models found no significant difference in odds of catch-up growth by maternal sedentary or MVPA trajectory groups (**Table 3**). While non-significant, odds of catch-up growth increased by increasing maternal sedentary and increasing maternal MVPA trajectories. Odds of catch-up growth in the medium and high maternal sedentary group were greater than the low group: unadjusted rates of catch-up growth occurrence were 1/9 (11%) in low, 5/26 (19%) in medium, and 8/25 (32%) in high. Odds of catch-up growth also nonsignificantly increased by increasing maternal MVPA trajectory with 1/15 (7%) catch-up growth cases occurring in low, 8/32 (25%) in medium, 5/13 (38%)in high.

Table 3. Odds of BMI Z-score Catch-up Growth by Maternal Sedentary Behavior and MVPA Trajectories

	Low		Medium		High	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Sedentary Trajectories	1.00 (reference)	-	1.90 (0.19, 18.93)	0.582	3.76 (0.40, 35.44)	0.247
MVPA Trajectories	1.00 (reference)	-	4.67 (0.53, 41.32)	0.166	8.75 (0.86, 88.69)	0.066

Unadjusted logistic regression models for trimester-specific maternal sedentary behavior and MVPA are presented in **Table 4**. Higher maternal MVPA was significantly associated with higher odds of catch-up growth in the second (OR 3.65, 95% CI 1.50, 8.82) and third (OR 2.16, 95% CI 1.12, 4.17) trimesters. First trimester activity was not related to odds of catch-up growth. Maternal sedentary behavior was not significantly associated with odds of catch-up growth in any trimester of pregnancy.

Table 4. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months by Trimester-Specific Maternal Sedentary Behavior and MVPA

	Trimester 1		Trimester 2		Trimester 3	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Sedentary Behavior	1.29 (0.66, 2.56)	0.452	0.88 (0.45, 1.72)	0.713	1.46 (0.70, 2.86)	0.327
MVPA	1.40 (0.77, 2.53)	0.271	**3.65 (1.50, 8.82)**	**0.004**	**2.16 (1.12, 4.17)**	**0.022**

Odds ratios represent odds of catch-up growth associated with a one standard deviation increase in sedentary behavior or MVPA
SD Sedentary: Trimester 1: 87.2 Trimester 2: 75.8 Trimester 3: 81.2 minutes
SD MVPA: Trimester 1: 16.6 Trimester 2: 17.3 Trimester 3: 17.3 minutes

Due to the small sample size in this analysis, all models are presented as unadjusted. Statistical significance and direction of effect were unaffected by including confounding covariates one at a time including adjustment for gestational age, which was significantly lower in children who did versus did not experience catch-up growth (data not shown).

4.2.2 Growth Rate

Predicted slopes of childhood BMI z-score growth by maternal sedentary and MVPA trajectories are displayed in **Figure 8**. To examine growth rate, mixed linear models including all child anthropometric data abstracted from medical records from birth up to 24 months tested for differences in slope of BMI z-score change with increasing age by maternal activity trajectory (n=62 children; mean: 9.2 observations per child). These analyses found that growth rate was significantly different by maternal sedentary, but not MVPA, trajectory. Both medium and high maternal sedentary trajectories had children with significantly steeper growth rates as compared to infants from mothers in the low sedentary trajectory. Participants in the high sedentary group

had the smallest BMI z-score at birth (BMI z-score low: 0.02, medium: -0.57, high: -1.10) and steepest slope of growth (slope: 0.080Δ BMI z-score/month) with increasing age.

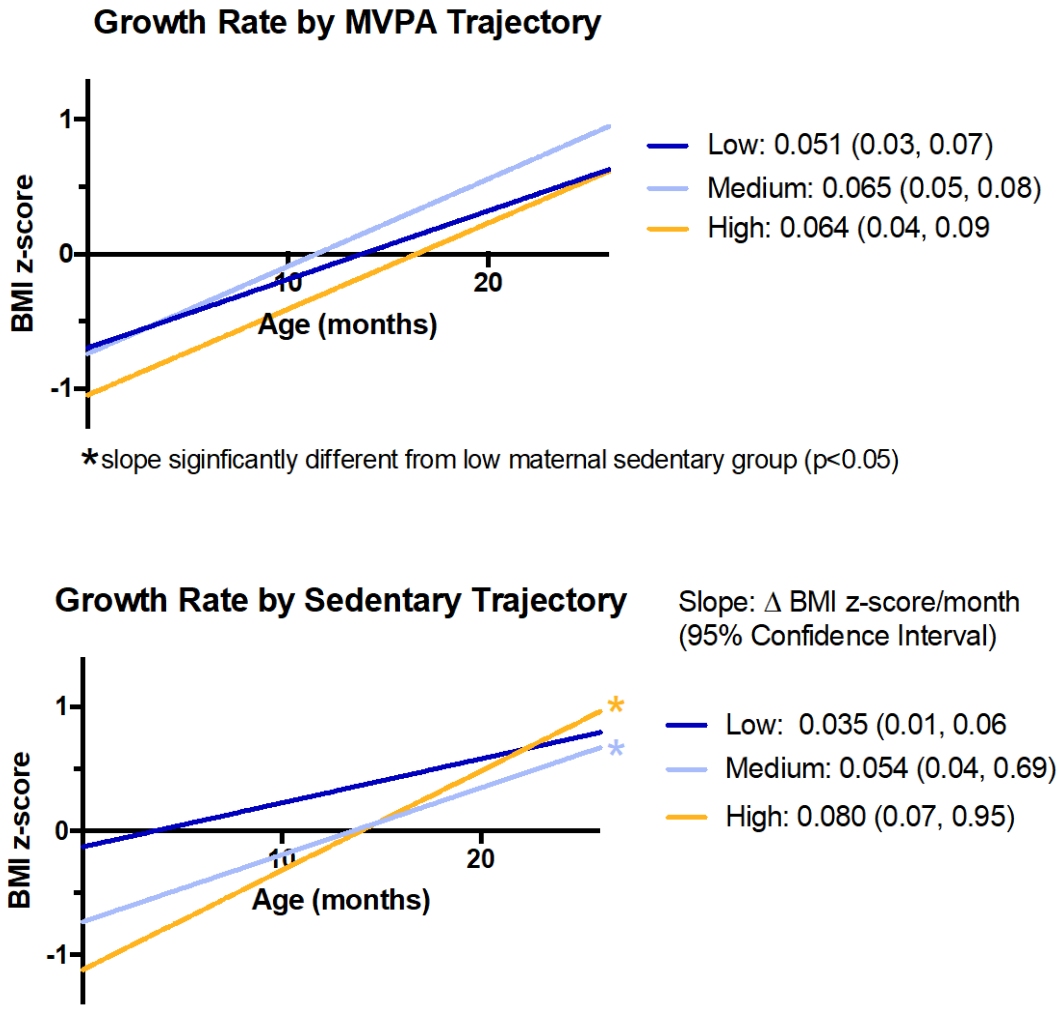

Figure 7. Incremental Rate of BMI Z-Score Change by Sedentary and MVPA Trajectory

Mixed linear models examining growth rate and trimester-specific maternal sedentary behavior and MVPA are displayed in **Table 5**. Higher sedentary time in the first trimester (std ß: 0.017, p= 0.001) as well as higher MVPA in the second (std ß: 0.013, p= 0.019) and third (ß: 0.011, p= 0.009) trimester were associated with steeper slope of growth.

Table 5 Incremental Rate of BMI Z-Score Change with Age by Trimester Specific Maternal Sedentary and MVPA

	Trimester 1		Trimester 2		Trimester 3	
	Std. Coef.	p-value	Std. Coef.	p-value	Std. Coef.	p-value
Sedentary Behavior	**0.017**	**0.001**	-0.002	0.725	0.004	0.350
MVPA	0.003	0.570	**0.013**	**0.019**	**0.011**	**0.009**

SD Sedentary: Trimester 1: 87.2 Trimester 2: 75.8 Trimester 3: 81.2 minutes
SD MVPA: Trimester 1: 16.6 Trimester 2: 17.3 Trimester 3: 17.3 minutes

Relevant participant characteristics were added to each model to test for influence. Inclusion of feeding type in models strengthened associations of sedentary time and rate of BMI z-score growth; other covariates did not impact statistical significance or magnitude of effect (data not shown).

4.3 Specific Aim 2

The second aim of this study examined how maternal activity profile during pregnancy relates to early childhood motor development. The primary method of motor development measurement was the Early Motor Questionnaire (EMQ). The questionnaire provides scores in three domains of motor development: gross motor, fine motor, and perception action. Secondarily, associations between maternal activity profile and self-reported child age of crawling and walking onset were assessed.

4.3.1 Early Motor Questionnaire

EMQ data were available for n=70 children between 13 and 30 months of age. Associations of the child's EMQ domain scores (gross motor, fine motor, and perception action) with participant characteristics can be found in **Supplemental Table 3** in Appendix G. Gross motor score was positively associated with maternal pre-pregnancy BMI and, in the subset of women with postpartum scores available, inversely associated with maternal Edinburgh postnatal depression scores. Perception action scores significantly differed by race, with the highest scores in White participants (49.1 [8.7]) and lowest in Black participants (33.2 [7.1]).

Linear regression models are presented in **Table 6** including associations with raw EMQ scores (with covariate adjustment for age, i.e., age-adjusted models) and separately using age-standardized EMQ scores as the outcome. Maternal sedentary behavior trajectory was not significantly associated with gross motor, fine motor, or perception action scores. In age-adjusted models, maternal MVPA trajectory was significantly associated with fine motor and perception action scores. Compared to the children with mothers in the low MVPA group, fine motor scores were 11.00 and 13.76 points higher in the children with mothers in the medium or high groups, respectively (both $p<0.05$). Children with mothers in the medium or high MVPA groups had higher perception action scores 7.02 and 9.56 points compared with children of mothers in the low group, respectively ($p<0.05$). All significant differences in scores correspond to a moderate effect sizes (semipartial correlation >0.20).

The secondary analysis approach using EMQ age-standardized scores did not yield significant associations with maternal activity profile trajectories. However, age-standardized associations of maternal MVPA trajectory with the child's fine motor and perception action were consistent with age-adjusted models in direction and magnitude with similar effect size.

Table 6. Association of EMQ Domains with Maternal Sedentary and MVPA by Trajectory Groups

	Low		Medium			High		
	Coef.	p-value	Coef.	p-value	ßstdXY	Coef.	p-value	ßstdXY
Sedentary Trajectories								
Gross Motor								
Age-adjusted	Reference	-	-3.74	0.464	0.094	-4.11	0.423	0.104
Age-standardized	Reference	-	-2.76	0.291	0.182	-2.71	0.300	0.179
Fine Motor								
Age-adjusted	Reference	-	-4.87	0.360	0.123	-6.11	0.254	0.155
Age-standardized	Reference	-	-7.28	0.084	0.295	-7.29	0.084	0.296
Perception Action								
Age-adjusted	Reference	-	-1.82	0.637	0.063	-4.18	0.280	0.146
Age-standardized	Reference	-	1.74	0.647	0.079	0.087	0.982	0.004
MVPA Trajectories								
Gross Motor								
Age-adjusted	Reference	-	0.31	0.941	0.008	5.33	0.307	0.102
Age-standardized	Reference	-	-0.57	0.793	0.038	2.17	0.422	0.289
Fine Motor								
Age-adjusted	Reference	-	**11.00**	**0.011**	0.282	**13.76**	**0.009**	0.283
Age-standardized	Reference	-	5.48	0.118	0.225	7.75	0.077	0.255
Perception Action								
Age-adjusted	Reference	-	**7.02**	**0.025**	0.247	**9.56**	**0.013**	0.271
Age-standardized	Reference	-	6.10	0.052	0.280	7.31	0.060	0.269

Age-adjusted models adjust for age of child at date of EMQ completion
Age-standardized models use EMQ score standardized to age
ßstdXY: Semipartial correlation represents effect size in which ß<0.2 is weak, 0.2<ß<0.5 moderate, and ß>0.5 strong effect

To illustrate average child EMQ scores across maternal activity profiles and using the age-adjusted model (primary analysis) presented in **Table 6,** predicted least square mean scores for each age-adjusted EMQ domain by maternal sedentary behavior and MVPA trajectories are presented in **Figure 8**. Predicted fine motor and perception actions scores were higher in the medium or high maternal MVPA trajectory groups compared to low maternal MVPA. Corresponding predicted scores can be found in **Supplemental Table 4** in Appendix G.

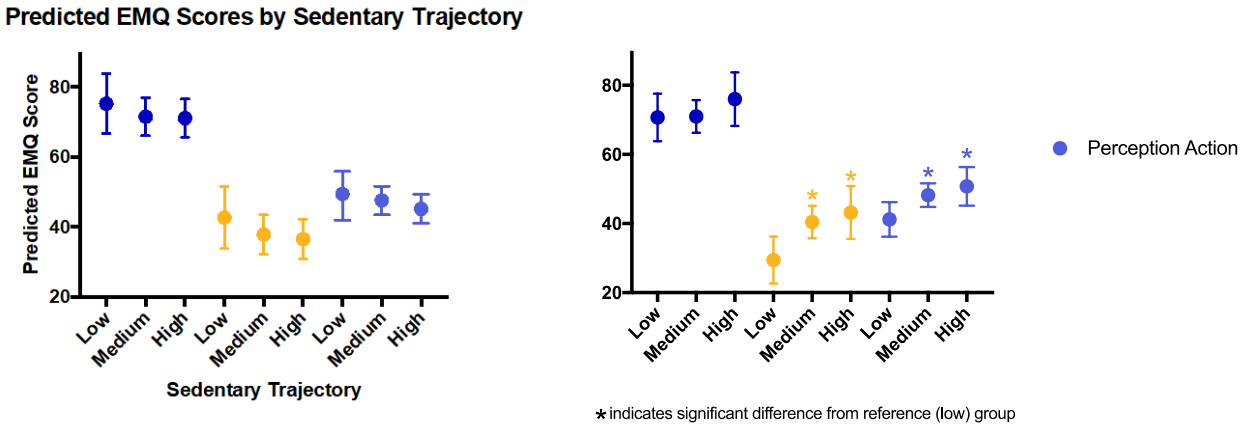

Figure 8. Predicted EMQ Scores by Activity Trajectories

Associations of the EMQ domain scores with trimester-specific sedentary behavior and MVPA are presented in **Table 7**. Consistent with the trajectory models, maternal sedentary behavior in any trimester was not associated with early childhood gross motor, fine motor, or perception action scores. Higher maternal MVPA in the first and second trimester was significantly associated with higher fine motor scores (first trimester std ß: 4.33, p=0.017, second trimester std ß: 3.72, p=0.044) in age-adjusted models. Higher MVPA in the first trimester was significantly related to higher perception action scores in the age-adjusted (std ß: 3.78, p=0.004) and age-standardized (std ß: 3.43, p= 0.008) models. In the second trimester, higher maternal MVPA was related to higher perception action score in the age-adjusted model only (std ß: 2.87, p= 0.031).

Relevant participant characteristics were added to each model to test for influence. Inclusion of pre-pregnancy BMI, race, Edinburg postpartum depression score, and other covariates one at a time did not change the statistical significance or magnitude of association in any statistical models (data not shown).

Table 7 Association of EMQ Domains with Trimester Specific Maternal Sedentary and MVPA

	Trimester 1		Trimester 2		Trimester 3	
	Std. Coef.	p-value	Std. Coef.	p-value	Std. Coef.	p-value
Sedentary Trajectories						
Gross Motor						
Age-adjusted	-2.10	0.246	-2.50	0.166	-1.55	0.400
Age-standardized	-1.88	0.203	-1.44	0.122	-0.69	0.469
Fine Motor						
Age-adjusted	0.26	0.894	-1.92	0.310	-1.96	0.317
Age-standardized	-0.36	0.815	-1.01	0.505	-1.95	0.213
Perception Action						
Age-adjusted	-1.35	0.327	-1.36	0.322	-0.79	0.580
Age-standardized	-0.41	0.765	-1.19	0.384	0.39	0.781
MVPA Trajectories						
Gross Motor						
Age-adjusted	1.90	0.279	0.29	0.873	-1.03	0.579
Age-standardized	0.99	0.276	-0.01	0.990	-0.67	0.488
Fine Motor						
Age-adjusted	**4.33**	**0.017**	**3.72**	**0.044**	2.70	0.171
Age-standardized	2.09	0.158	2.68	0.073	2.58	0.108
Perception Action						
Age-adjusted	**3.78**	**0.004**	**2.87**	**0.031**	1.42	0.330
Age-standardized	**3.43**	**0.008**	1.62	0.228	0.01	0.992

Std. Coef: Coefficient representing change in EMQ score per 1 SD change sedentary or MVPA
SD sedentary: Trimester 1: 87.2 Trimester 2: 75.8 Trimester 3: 81.2 minutes
SD MVPA: Trimester 1: 16.6 Trimester 2: 17.3 Trimester 3: 17.3 minutes
Sedentary Behavior Trimester 1: n=58 Trimester 2: n=58 Trimester 3: n=55
MVPA Trimester 1: n=60 Trimester 2: n=59 Trimester 3: n=55

4.3.2 Crawling and Walking Onset

As a secondary measure of motor development, linear regression models tested the associations between maternal sedentary behavior and MVPA trajectories with mother-reported age of crawling and walking onset. **Figure 9** presents the predicted onset age of crawling and walking by sedentary behavior and MVPA trajectories. Mean (SD) age of crawling and walking onset was 7.5 (1.5) months and 12.4 (1.7) months, respectively. At the time of questionnaire completion, n=2 participants were not able to walk independently and unaided. Recall of crawling age was reported based on memory (48%), dated video or picture (44%), or diary, social media, or other calendar (8%). Recall of walking age was reported based on memory (55%), dated video or picture (30%), or diary, social media, or other calendar (15%). Being in the medium maternal MVPA trajectory was significantly associated with a later crawling onset age compared to the low MVPA group (7.79 versus 6.94 months); no other significant associations were observed. While not statistically significant, age of walking onset appeared to be directly associated with higher maternal sedentary behavior trajectories and indirectly associated with higher MVPA trajectories, indicating a potential dose response association. Age of crawling or walking onset was not significantly associated with trimester specific sedentary behavior or MVPA (data not shown).

Analyses with trimester specific maternal activity profile did not reveal any unique associations compared to the activity trajectory models. Neither sedentary behavior or MVPA in any trimester was significantly associated with crawling or walking onset age (data not shown).

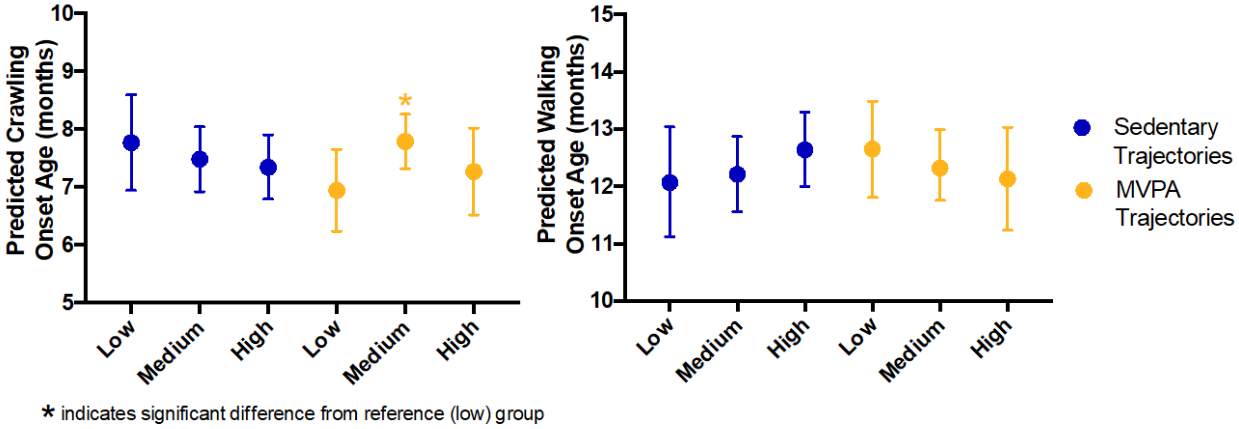

Figure 9. Predicted Age of Crawling and Walking Onset by Activity Trajectories

4.4 Exploratory Aim

Analyses were conducted to examine the importance of BMI z-score at birth for explaining the association between maternal sedentary behavior and MVPA with risk of catch-up growth and motor development. Incremental growth rate was not included in this exploratory aim as statistical models were already inclusive of BMI z-score at birth.

4.4.1 Catch-Up Growth

Results from the analyses of activity trajectory and risk of catch-up growth with and without adjustment for BMI z-score at birth are presented in **Table 8**. No sedentary behavior or MVPA trajectories were significantly associated with greater odds of catch-up growth in either model. However, the magnitudes of the odds ratios for catch-up growth in medium and higher sedentary behavior and MVPA trajectories were meaningfully attenuated with adjustment for BMI z-score at birth.

Table 8. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months of Age by Maternal Sedentary and MVPA Trajectory With and Without Adjustment for BMI Z-Score at Birth

	Low		Medium		High	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Sedentary Behavior						
Unadjusted	1.00 (Reference)	-	1.90 (0.19, 18.92)	0.581	3.76 (0.40, 35.44)	0.247
Adjusted	1.00 (Reference)	-	0.91 (0.06, 13.98)	0.948	0.97 (0.06, 14.72	0.981
MVPA						
Unadjusted	1.00 (Reference)	-	4.67 (0.53, 41.32)	0.166	8.75 (0.86, 88.69)	0.066
Adjusted	1.00 (Reference)	-	2.26 (0.22, 23.66)	0.497	3.24 (0.23,44.01)	0.377

Adjusted models include BMI z-score at birth

Results from the analysis of trimester specific maternal activity and risk of catch-up growth with and without adjustment for BMI z-score at birth are presented in **Table 9**. Statistically significant unadjusted associations of MVPA with risk of catch-up growth were no longer significant with the addition of BMI z-score at birth. In the second trimester, odds of catch-up growth was reduced from 3.65 to 2.30. In the third trimester, odds were reduced from 2.16 to 1.69.

Table 9. Odds of BMI Z-Score Catch-Up Growth Between Birth and 12 Months of Age by Trimester Specific Activity With and Without Adjustment for BMI Z-Score at Birth

	Trimester 1		Trimester 2		Trimester 3	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Sedentary Behavior						
Unadjusted	1.29 (0.67, 2.48)	0.452	0.88 (0.45, 1.72)	0.713	1.42 (0.70, 2.86)	0.327
Adjusted	0.78 (0.32, 1.86)	0.560	0.49 (0.18, 1.39)	0.180	1.18 (0.49, 2.85)	0.715
MVPA						
Unadjusted	1.40 (0.77, 2.54)	0.271	**3.65 (1.51, 8.82)**	**0.004**	**2.16 (1.12, 4.15)**	**0.022**
Adjusted	1.06 (0.49, 2.29)	0.877	2.30 (0.77, 6.88)	0.137	1.69 (0.74,3.85)	0.211

Adjusted models include BMI z-score at birth

4.4.2 Motor Development

Associations between maternal activity trajectories and EMQ scores, before and after adjustment for infant birth BMI z-score, are presented in **Table 10**. Participants that did not have both valid EMQ data and BMI z-score data were excluded from this analysis resulting in an analytical sample of n=59.

Association between all EMQ score domains and maternal sedentary behavior trajectory were nonsignificant and similar with and without adjustment for infant BMI z-score at birth. Higher maternal MVPA was similarly and nonsignificantly associated with gross motor score with and without adjustment for BMI z-score at birth. High maternal MVPA trajectory was significantly associated with higher fine motor score with and without adjustment for BMI z-score at birth, and, in fact, adjusted associations were typically strengthened. Higher perception action score was significantly associated with high maternal MVPA trajectory prior to adjustment for BMI z-score at birth; though the magnitude of association was strengthened, the association was no longer statistically significant after adjustment.

Table 10. Associations Between Activity Trajectories and EMQ Scores With and Without Adjustment for BMI Z-Score at Birth

	Low		Medium		High	
	Coef.	p-value	Coef.	p-value	Coef.	p-value
Sedentary Trajectories						
Gross Motor						
Model 1	Reference	-	-2.07	0.734	-1.63	0.788
Model 2	Reference	-	-1.96	0.754	-1.43	0.825
Fine Motor						
Model 1	Reference	-	-4.65	0.400	-3.39	0.538
Model 2	Reference	-	-5.19	0.359	-4.38	0.454
Perception Action						
Model 1	Reference	-	-1.01	0.824	-2.77	0.544
Model 2	Reference	-	-1.59	0.733	-3.83	0.429
MVPA Trajectories						
Gross Motor						
Model 1	Reference	-	-0.95	0.845	3.57	0.552
Model 2	Reference	-	-0.70	0.887	4.09	0.515
Fine Motor						
Model 1	Reference	-	7.22	0.094	**11.60**	**0.031**
Model 2	Reference	-	7.36	0.094	**11.91**	**0.034**
Perception Action						
Model 1	Reference	-	5.38	0.133	**8.80**	**0.048**
Model 2	Reference	-	5.43	0.138	8.90	0.056

Model 1 includes adjustment for age splines
Model 2 includes adjustment for age splines and BMI z-score at birth

Trimester specific maternal activity profile was not associated with EMQ domain scores in any trimester when excluding those that did not have BMI z-score at birth. Addition of BMI z-score at birth to models did not impact the statistical significance or magnitude of associations (data not shown).

5.0 Discussion

5.1 Summary of Findings

This study was conducted to better understand how maternal activity profile across pregnancy may relate to early childhood growth and development. Previous research suggests that maternal activity profile during pregnancy may impact fetal growth *in utero.* Little is known about whether this effect persists after birth to impact growth and development of the offspring in early life. To address this research gap, we conducted a longitudinal follow-up study of the children born to mothers enrolled in our previous cohort study which measured objective activity patterns across each trimester of pregnancy.

We found that higher maternal MVPA, specifically in later pregnancy, was associated with increased odds of catch-up growth in the child at one year of age and a faster rate of increase in BMI z-score from birth up to 24 months of follow-up. Maternal sedentary behavior was not associated with odds of catch-up growth, though higher sedentary time, specifically in the first trimester, was associated with a more rapid slope of BMI z-score increase over follow-up. Associations of activity profile and catch-up growth were attenuated with adjustment for BMI z-score at birth.

Compared to low maternal MVPA, medium or high levels of maternal MVPA were also related to more advanced motor development, specifically higher fine motor and perception action scores at 13-30 months of age. Sedentary behavior was not significantly related to motor development. Results were unchanged in magnitude and direction of association with adjustment for BMI z-score at birth, suggesting an independent effect.

5.2 Catch-Up Growth and Growth Rate

We hypothesized that lower sedentary time and higher MVPA during pregnancy would be related to less catch-up growth from birth to 12 months and a more stable rate of growth up to 24 months in the offspring. Contrary to our hypothesis, we found that being in the high maternal MVPA trajectory was associated with higher odds of catch-up growth in the child. Considering the evidence that catch-up growth is associated with cardiovascular disease risk[33,34,45,91] and overweight and obesity risk,[10,11,31] our findings suggest that higher levels of maternal MVPA may have a deleterious effect on long-term health of the offspring. However, further consideration of growth patterns may be necessary to interpret these findings. BMI z-score at birth was not associated with maternal MVPA trajectory in this cohort, and some studies have suggested that catch-up growth, in the absence of small birth size, is not as strongly associated with long-term poorer health.[33,45] It is important to note that physical activity during pregnancy is considered safe and encouraged in healthy, uncomplicated pregnancies.[49] Therefore, our findings do elicit further investigation into the long-term impact that higher levels of maternal activity may have on offspring, specifically, whether associated catch-up growth in these offspring results in deleterious long-term health outcomes in broader population studies.

To the best of our knowledge, this is the first study to objectively measure activity in pregnancy with follow-up that assesses within-subject changes in offspring BMI z-score in early childhood. However, our results can be compared to previous studies which have reported on differences in offspring body mass between experimental and control groups following antenatal exercise interventions at various time points in childhood. In one randomized control trial, 84 previously inactive women were randomized to either a 12-week exercise intervention (n=47) in the second and third trimester, including five 45-minute aerobic exercise sessions per week, or a

control condition (n=37). Anthropometric measures were then collected on children at birth, one year (intervention: n=38, control: n=23) and seven years (intervention: n=33, control: n=24) of follow-up. This study found lower birthweight, no difference in weight at one year follow-up, and higher body fat percentage at seven years follow-up in offspring from the experimental versus control groups.[77] While within-subject changes in infant weight were not directly reported, birthweight was lower in the intervention offspring but did not differ from controls at one year. This may be indicative of similar growth patterns to our findings in which MVPA, especially in the second and third trimester, was related to a quicker rate of growth and higher risk of catch-up growth. Contrasting our findings, another study selected 40 physically active women, 20 of which voluntary stopped exercising during pregnancy and a matching 20 other women who had engaged in at least 30 minutes of MVPA three or more times per week during pregnancy. Follow-up on the children born to mothers in this study at five years found lower body fat percentage in the exercising group versus active controls.[76] Lastly, a randomized controlled trial, which included dietary counseling and 30 to 60 minutes of daily unsupervised moderate aerobic activity in overweight and obese women, assessed child anthropometrics (intervention: n=77, control: n=73) between 2.5-3 years of age. This study found no difference in offspring BMI z-score at follow-up.[78] The differences in populations and methodology between the existing studies make it difficult to compare findings. Yet, taken together, maternal physical activity may have an effect on risk for catch-up growth. However, this effect may vary by time of exercise introduction, pre-pregnancy activity, age of follow-up on the children, and maternal BMI.

To the best of our knowledge, our study is the first to examine the effects of sedentary behavior in pregnancy on catch-up growth or rapid growth. Offspring of women with higher amounts of sedentary time were born smaller, and, particularly for those women with high

sedentary time in the first trimester, were more likely to have rapid growth up to 24 months. Rapid growth, when accompanied by small size at birth, is associated with a higher long-term risk for cardiovascular disease, overweight, and obesity.[33,45] Therefore, the potential negative impact of high sedentary time during early pregnancy on long-term health of the offspring requires further investigation.

Due to the nature of this study, the mechanisms by which maternal MVPA or sedentary behavior may result in catch-up or rapid growth cannot be ascertained. One proposed mechanism by which this may occur is the mismatch theory (described in detail in Chapter 2, Section 2.1). This theory suggests that differences between *in utero* and postnatal nutritional availability result in a metabolic mismatch[66,67] that may lead to quicker rate of growth postnatally. The effects of maternal sedentary behavior and MVPA on nutrient availability during pregnancy could lead to a mismatch in pre- and postnatal environments, resulting in less healthy growth patterns during early childhood.

MVPA in early pregnancy is related to increased placental volume and vascularization, which would in turn relate to improved nutrient delivery to the developing fetus.[131] A review of the long-term offspring implications of exercise in pregnancy also suggests intermittent reductions in maternal glucose after exercise, specifically in late pregnancy, may result in placental adaptations and reduced nutrient delivery to the fetus overtime.[132] This suggests that higher MVPA in late pregnancy may reduce nutrient delivery to the fetus, which would generally be considered an adverse effect (except in the presence of hyperglycemia or GDM). However, MVPA during pregnancy is consistently associated with a reduction of risk of a large for gestational age (LGA) birth without increasing the risk of small for gestational age. (SGA).[20-24] Taken together, these data then suggest that MVPA may be protective of a nutritional excess to the fetus during late pregnancy

and, when matched with abundant nutrition postnatally, may increase the offspring's risk for catch-up or more rapid growth.

Further, our findings in which higher sedentary behavior, specifically in early pregnancy, was related to more rapid growth rate could be explained by the same mismatch theory. Rather than exercise drawing nutrients away from the fetus, the placenta's vascular capacity to transport nutrition to the fetus may be reduced with high amounts of sedentary time.[17] This proposed mechanism is consistent with previous findings from our group in which high maternal sedentary time was related to smaller ponderal index at birth. One previous study of 206 individuals found that lower ponderal index was related to lower oxygen tension, a measure of blood flow and sufficiency of nutrient delivery, in the placenta.[105] Insufficient early pregnancy nutrient delivery may inhibit the structure and function of developing organ systems, preparing the fetal physiology for less nutrition than what is then available postnatally.

Lastly, our findings could also be related to postnatal exposures rather than *in utero* programming. While factors such as feeding type, primary caregiver interactions, and maternal diet have not been directly related to catch-up growth, they are related to childhood health.[55] Further, birth size and early childhood weight gain differ by maternal education, race, and socioeconomic status.[110,111] Due to our small sample size and lack of racial and economic diversity, our ability to adjust for covariates was limited. However, the addition of available covariates to models did not change the significance or magnitude of associations. Our findings in which BMI z-score at birth attenuated the associations between maternal MVPA and catch-up growth would support *in utero* development increasing the risk of catch-up growth as opposed to postnatal exposures. Further research on postnatal correlates of catch-up growth are needed to disentangle fetal programming or postnatal environmental factors as mechanisms for catch-up growth.

Overall, these data suggest that activity patterns during pregnancy may have an effect on early childhood growth rates. Currently, physical activity during pregnancy is considered safe and encouraged due to multiple maternal-child benefits such as reduced risk for adverse pregnancy outcomes, cesarean delivery, and LGA birth size.[49] There are no recommendations for sedentary behavior, though increased attention to the potentially deleterious effects of excessive sedentary behavior on pregnancy and general health will inform future recommendations in the coming decades.

5.3 Motor Development

We hypothesized that higher maternal sedentary time and lower MVPA would relate to poorer motor development in early childhood. Our hypothesis was partly confirmed as higher levels of MVPA were related to more advanced fine motor (small muscle group control) and perception action (physical response to visual stimuli) scores between 13-30 months of age. On the other hand, being in the medium trajectory of MVPA, compared to low or high, was associated with later onset age of crawling. Sedentary behavior was not significantly associated with motor development scores in early childhood. Motor development is foundational for a child's physical, social, and psychological health.[79] Poorer motor development may have long-term consequences as it has been related to an increased risk for obesity and lower levels of MVPA in childhood.[36,37] These findings indicate that engaging in MVPA during pregnancy may have short- and long-term benefits for the child's motor development and future physical activity.

Few studies have examined the association between maternal MVPA in pregnancy and child motor development. Of the existing studies, measurement of development varies greatly

including cognitive, language, motor, and intelligence domains, making it difficult to compare findings.[84-86,133] In one observational cohort study most similar to our study, including 528 pregnant women, self-reported maternal leisure time physical activity in each trimester was collected and the Bayley Scales of Infant and Toddler Development was used to measure development of children at 1- and 2-years follow-up. This study found no difference in the motor development score across maternal physical activity levels in children at either follow-up timepoint.[124] This cohort study differs from ours by measurement methodology for both physical activity and child development. Our study objectively measured MVPA and included all domains of MVPA accumulated throughout the day, while this study used self-reported leisure time physical activity only. Including all activity accumulated across the day may have provided a more sensitive and biologically relevant measure of overall physical activity habits, which in turn may be more strongly related to motor development than leisure time physical activity alone. Another difference in methodology was their measure of motor development was directly assessed by trained research staff using a stronger measure of motor development than our parent-reported questionnaire.

The association between maternal MVPA and child motor development has also been tested experimentally, with most studies finding no significant association. One structured exercise program included one in-person 60-minute exercise session and two at home 45-minute sessions of aerobic and strength exercise per week between 20-36 weeks of pregnancy. This study then compared developmental scores of children (intervention: n=164, control: n=115) at 7 years of age using the 'Five-to-Fifteen' motor development questionnaire. The results of this study found no difference in fine or gross motor score domains between children born to mothers in the intervention compared to the control groups.[85]

Further, another randomized controlled trial which also included one in-person and two at home 45-minute per week, but limited to aerobic exercise only, (intervention: n=188, control n=148) measured development using Bayley Scales of Infant and Toddler Development in children at 18 months old. There were no significant differences in overall motor development scores between intervention and control groups. However, while non-significant, children of mothers in the exercise intervention had lower motor scores than controls. Further, in subgroup analyses by sex, this difference became significant in boys only.[86] It is important to note that, according to the authors, these differences in scores do not appear to be clinically meaningful. Lastly, and contrary to other findings, a small supervised exercise trial including three 50-minute moderate intensity aerobic exercise sessions per week with 27 intervention and 33 control participants measured motor development of children using the Peabody Developmental Motor Scales at one-month follow-up. This study found that, at one-month old, children born to the intervention mothers had significantly higher locomotion scores than controls.[84] Scores were also higher for stationary and gross motor domains compared to controls but were not statistically significant. Overall, these studies differ from ours by the use of experimental manipulation of exercise. Our observational design may capture more habitual exercise which may explain the different findings. Further, the varying age of follow-up and motor development measurement tools in the existing literature makes comparison difficult. Taken together, habitual exercise may have a positive impact on early childhood motor development, while introducing activity during pregnancy may have no effect or only short-term benefit[84] on motor development. Further investigation is needed to better understand the short- and long-term developmental implications of MVPA during pregnancy.

To the best of our knowledge this is the first study to examine the association between maternal sedentary behavior. Therefore, our findings in which maternal sedentary behavior, across

pregnancy or in any trimester, did not relate to early childhood gross motor, fine motor, or perception action cannot be put into a broader context for comparison. However, our data do offer novel evidence that maternal sedentary behavior does not appear to impact early childhood motor development due to the small magnitude and non-significance of associations observed.

Further, no previous studies have examined associations between maternal activity profile and crawling or walking onset age. Though statistically nonsignificant, age of walking onset appeared to be directly associated with higher maternal sedentary behavior trajectories and indirectly associated with higher MVPA trajectories, indicating a potential dose response association. Our findings in which being in the medium MVPA trajectory, compared to low or high, was related to a later age of crawling onset contrast our other findings in which MVPA was related to more advanced development. However, the difference in crawling onset age (7.79 versus 6.94 months) may not being clinically meaningful. Also, retrospective recall error in crawling onset age may be one explanation for this association. These findings warrant further investigation.

While we cannot say for certain the mechanisms by which MVPA in pregnancy may lead to more advanced motor development in early childhood as we did not formally study these, we propose two possibilities. The first is related to the Developmental Origins of Health and Disease theory. This theory would posit that higher levels of MVPA, primarily in early pregnancy, could aid in improved fetal development. Early pregnancy is when the structure and function of organ systems are being developed, as opposed to late pregnancy when fetal growth is primarily body fat development. Maternal MVPA during pregnancy is associated with improved nutrient sensing and vascularization of the placenta.[18,19] Improved nutrient transport in early pregnancy may relate to more optimal development of musculoskeletal and organ systems *in utero* which may allow for more advanced motor development in childhood. This could be consistent with our findings in

which adjustment for BMI z-score at birth did not explain the associations between maternal MVPA and fine motor and perception action scores. This suggests any effect of MVPA in late pregnancy would impact fat deposition and soft tissue growth, which was no longer associated with motor development in our analysis. Therefore, the early pregnancy effects on musculoskeletal and organ system development related to MVPA may be a plausible mechanism by which higher MVPA relates to improved motor development.

The second proposed mechanism is postnatal exposure (i.e., 'nurture'). Our study was observational in nature and, therefore, likely captured habitual exercise. Although not measured in this study, those with high levels of MVPA during pregnancy may be more likely to be physically active postpartum. Further, we propose that women who are more active themselves may also be more active with their child, which would encourage motor developmental behaviors. However, evidence supporting a direct relationship between parental activity and child motor development is limited. More advanced motor development has been associated with higher levels of physical activity in children[99] and physically active parents are more likely to have physically active children.[134] One study found that higher levels of paternal, not maternal, accelerometer-measured MVPA was associated with improved motor development in 846 preschool aged children.[135] In contrast, another observational study actually found that maternal self-reported physical activity was related to poorer object control, a domain of motor development in the Test for Gross Motor Development-2.[136] Though plausible, current data do not draw a clear link between maternal physical activity in pregnancy or post-partum with motor development in children. Further studies are needed to elucidate the mechanism by which maternal MVPA may relate to motor development. Future research should examine environmental and social determinants of childhood motor development as well as the examination of physiological differences or biomarkers related

to improved motor development in order to differentiate between the effects of nature versus nurture.

Overall, maternal activity occurring early in pregnancy may relate to more advanced motor development while introduction of activity later in pregnancy may not have an effect. The mechanism by which this may occur remains uncertain. Further, maternal sedentary behavior does not appear to relate to motor development, but more evidence is needed as our study has limitations in size and rigor and was the first to examine this association.

5.4 Strengths and Limitations

The primary strength of this study was the objective measurement of sedentary time and physical activity across all trimesters of pregnancy. Having multiple measures during pregnancy allowed for analysis by pattern across pregnancy and by each trimester. Further, the prospective, observational design allowed for assessment of habitual sedentary behavior and MVPA and the ability to establish temporality of the prenatal exposures with postnatal outcomes. Other strengths include data collection from medical records which included anthropometrics objectively measured by clinicians. This also allowed for analyses using multiple measurement time points for each subject to get a more accurate measure of growth rate during early childhood.

This study also had limitations. The small sample size and limited racial, educational, and socioeconomic diversity affected our ability to adjust for possible confounders in our analyses. While adjustment for these variables one at a time did not change our results, this could be attributed to a lack of power to detect differences. We also had limited ability to adjust for confounders as there was minimal variability within sociodemographic variables commonly

controlled for in other studies. As discussed in Chapter 2, Section 2.4, there are documented racial, socioeconomic, and educational differences in birth size and growth rate. The results found in our study may differ in mothers and children of racial/ethnic minority groups and our inability to stratify findings or control for these potential confounders limits the generalizability.

Another limitation of this study is the use of parent-reported motor development using the Early Motor Questionnaire. While this tool is considered valid and reliable compared to objectively-measured motor development tools, there is the risk of bias or misrepresentation of motor development ability with parent report. Over- or under-reporting of motor development by the mothers could have influenced our results. Further, this questionnaire was also collected in a non-systematic time frame (from 13 to 30 months), and sometimes outside of the optimized window (after 24 months old). Lastly, due to the observational nature of this study, we cannot determine causality of our findings. As we did not experimentally manipulate maternal activity patterns during pregnancy, we cannot say for certain that changing sedentary time or MVPA would elicit the same effects. However, despite these limitations, our findings inspire future study of the association between maternal activity profiles and early childhood growth and development.

5.5 Future Directions

Though our findings that activity profile relates to early childhood growth and motor development adds to the current Developmental Origins of Health and Disease literature, more evidence is needed in several areas. First, studies with longer follow-up on childhood health outcomes are needed. The long-term implications of catch-up growth in the absence of small birth size as well as differences in motor development in early childhood are needed to ascertain whether

the benefits or detriments of MVPA in pregnancy are clinically meaningful. Next, in order to understand the mechanisms by which activity in pregnancy relate to short- and long-term health of the offspring, studies should aim to disentangle the impact of *in utero* and postnatal exposures. Examination of postnatal determinants of catch-up growth or motor development, biomarkers and physiological differences in children at birth by maternal activity, and experimental manipulation of modifiable factors related to these childhood health outcomes are needed to gain clarity on these mechanisms and to inform intervention design. Further, more rigorous measurement of motor development by trained researchers using validated tools as well as measurement at systematic time points across childhood are design elements that could more precisely measure outcomes and improve future studies. Evidence in larger and more diverse samples but maintaining the objective measures of sedentary behavior and MVPA during pregnancy is also needed to confirm our findings and to determine if our findings differ by important sociodemographic factors. Understanding whether our findings persist across more diverse populations is critical to inform culturally sensitive and tailored interventions or recommendations regarding activity in pregnancy. Further, a better understanding of the optimal maternal activity profile for offspring health is needed. This could include further examining maternal activity intensities (light, moderate, or vigorous) or type (occupational or leisure time physical activity) to understand potential differential effects on childhood health outcomes. Additionally, studies including experimental manipulation of sedentary behavior and MVPA in pregnancy are needed to determine if changing these behaviors results in improved growth or development of the offspring. This could include exercise interventions to increase MVPA or interventions focused on reducing sedentary behavior.

5.6 Conclusions

There is substantial evidence to suggest that early life exposures and health are strongly related to health outcomes across the lifespan. Our findings indicate that maternal activity behaviors during pregnancy may have implications on early childhood health. Within the context of the Developmental Origins of Health and Disease theory, our findings propose modifiable prenatal exposures by which risk for non-communicable diseases of the offspring may be impacted. While the potential benefits of maternal MVPA for early childhood motor development are notable, the potential deleterious effects of higher levels of MVPA on risk for catch-up growth and more rapid growth warrant further investigation. Furthermore, high amounts of sedentary behavior were related to more rapid early childhood growth, adding to a growing body of evidence on the adverse effects of high amounts of sedentary time during pregnancy. This reinforces the need for sedentary behavior research and consideration of sedentary behavior recommendations for pregnant women. Overall, maternal activity profile shows promise as a modifiable risk factor to improve intergenerational health.

Appendix A

Recruitment Flyer

Appendix B

Screening Form

Screening

Please complete the survey below.

Thank you!

The following survey will be used to determine your eligibility for the MoM Health 2.0 study. Please answer the following questions only regarding the child born to you during your participation in the MoM Health Study (April 2017-April 2019).

Is your child >12 months old?	◯ Yes ◯ No
Does your child have any diagnosed chromosomal or congenital abnormalities that may affect growth or development?	◯ Yes ◯ No
(If yes) Briefly describe:	_____
Do you have legal custody of this child?	◯ Yes ◯ No

Appendix C

Demographic and Health Questionnaires

a. *What is the highest grade in school you have finished*? *(Check one)*
- ☐ Did not finish elementary school
- ☐ Finished middle school (8th grade)
- ☐ Finished some high school
- ☐ High school graduate or G.E.D
- ☐ Vocational or training school after high school
- ☐ Some College or Associate degree
- ☐ College graduate or Baccalaureate Degree
- ☐ Masters or Doctoral Degree (PhD, MD, JD, etc)

b. *What is your current marital status? (Check One)*
- ☐ Married
- ☐ Living in a marriage-like relationship
- ☐ Separated or divorced
- ☐ Widowed
- ☐ Single / Not Married

c. *What insurance covers most of your health care costs*?
- □ Medicaid
- □ Medicare
- □ Private (Blue Cross, UPMC, Health America, etc.)
- □ None
- □ Don't know

d. *What is your annual household income (in thousands)?* (read choices)
- ☐ Less than 10 thousand
- ☐ 10 to less than 20
- ☐ 20 to less than 35
- ☐ 35 to less than 50
- ☐ 50 to less than 75
- ☐ 75 to less than 100
- ☐ 100 to less than 150
- ☐ 150 or more
- ☐ Don't know
- ☐ Refused to answer

e. *Do you <u>currently</u> smoke tobacco on a daily basis, less than daily, or not at all?*
- ☐ Daily

- ☐ Less than daily
- ☐ Not at all
- ☐ Don't know

Please answer the following questions regarding the child you were pregnant with during your participation in the MoM Health Study

f. *Is your child of Hispanic or Latino origin?*
   - ☐ Yes
   - ☐ No

g. *Which race best describes your child? (Check all that apply)*
   - ☐ White or Caucasian
   - ☐ Black or African American
   - ☐ American Indian/Native American
   - ☐ Native Hawaiian or other Pacific Islander
   - ☐ Asian
   - ☐ Other: _____

h. *Which adults does your child primarily (>50% of the time) live with? (Check all that apply)*
   - ☐ With mother and father
   - ☐ Only mother
   - ☐ Only father
   - ☐ With mother and her partner
   - ☐ With father and his partner
   - ☐ With grandparents
   - ☐ Other adult(s) (please specify) _____

i. *On average, how many days per week does your child attend childcare?* _____ days

j. *On average, how many hours per day does your child attend childcare?* _____ hours

k. *How many persons live in the household where your child currently lives?*
   ___ ___ people

   a. (if ≥1) *How many of these are children under the age of 18?* ___ ___ *children*
      i. (if yes to children) *What are the ages of the children in your household?*
         Child 1: ___ ___ years
         Child 2: ___ ___ years
         Child 3: ___ ___ years
         Child 4: ___ ___ years
         Child 5: ___ ___ years
         Child 6: ___ ___ years

l. *What is your child's date of birth?* __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

m. *How old is your child?* ____ months

n. Does your child have any medical conditions for which they currently under the care of a doctor or other health professional?

Condition	What age was your child at the time of diagnosis?	Describe treatment

Appendix D

Breastfeeding Questionnaires

a) *Did you <u>ever</u> breastfeed your baby (or feed your baby your pumped milk)?*

☐NO → Skip to next questionnaire

☐YES → Continue

b) *Have you completely stopped breastfeeding and pumping milk for your baby?*

☐NO → Go to question d

☐YES → Continue

c) *How old was your baby when you completely stopped breastfeeding and pumping milk?*

_____ WEEKS **OR**_____ MONTHS

(if stopped breastfeeding) When you were breastfeeding or pumping milk for your baby, were you exclusively breastfeeding/pumping or did you supplement with formula?

☐Exclusive breastfeeding
☐Supplemented with formula

(if currently breastfeeding) Are you exclusively breastfeeding/pumping or do you supplement with formula?

☐Exclusive breastfeeding

☐Supplementing with formula

(if baby has received formula) How old in months was your baby when they started drinking formula?

☐Newborn

☐1 month

☐2 months

☐3 months

☐4 months

☐5 months

☐6 months

d) *Has your baby started eating solid foods?*

☐NO → Go to next questionnaire

☐YES → Continue

(if baby has received solid foods) How old in months was your baby when they started eating solid foods?

_____MONTHS

Appendix E

Early Motor Questionnaire

 Revision 1.6

Early Motor Questionnaire (EMQ)

Child's Lab ID: _____ Child's birthdate: Month:____ Day:____ Year:____

Chronological age: _____Months, _____Days Today's date: Month:____ Day:____ Year:____

Was your child born premature (<37 weeks gestation)? O Yes, at _____weeks of gestation O No, full term.

Relation to child: _____ Child's gender: O Male O Female

Do you have a child diagnosed with an Autism Spectrum Disorder? O Yes O No

Please read carefully before starting.

As you read each description of each behavior below, please indicate how certain you are whether your child already shows the described behavior or not. Please rate your certainty by circling one of the numbers in the right column. A 0 indicates that you are not certain whether your child shows this behavior or not. A -2 or 2 indicates that you are very certain and can recall a particular instance where your child showed this behavior.

Sure that child does NOT show behavior (e.g., you have seen your child fail when attempting this or a similar behavior)	**Child probably does NOT show behavior yet**	**Unsure whether child could do this or not** (please try to use this category seldom)	**Child probably shows this behavior**	**Sure that child shows this behavior and remember a particular instance**
-2	-1	0	1	2
You are sure that your child does not show this behavior yet. *You can recall a particular instance where you child has failed this or a related behavior.* *The behavior is not developmentally appropriate yet.*	*You cannot recall an instance where your child has attempted and failed this behavior, but your child does not show similar behaviors and you think he/she may not show this behavior yet.*	*You cannot recall an instance and you are not sure whether your child would show this behavior or not.* *Please use this category sparingly.*	*You cannot recall a particular instance but your child shows a similar behavior.* *Somebody (friend, nanny, daycare provider, other caretaker) has told you that your child shows this behavior*	*You have seen this behavior in your child.* *You recall a particular instance when the behavior occurred.* *Your child used to show this behavior but now shows more advanced behaviors (e.g., now walking instead of crawling)*

➔ When rating a behavior your child used to do but that is not developmentally appropriate anymore (e.g., crawling when the child is already walking alone) please rate this behavior as +2.

This questionnaire covers ages 2-24 months, there are behaviors listed your child **may not yet show (circle -2)**, or used to show but **may not be evident any more (circle +2)**.

Section 1: Gross motor skills

(49 items)

In the following please think about your child's gross motor skills and motor control. These skills relate to how easily your child is able to control his or her own movements, orient, obtain toys, or move around the room.

→ Skills are organized by posture and increase in difficulty within each posture.

When held up against your shoulder, your child will					
01) snuggle in and rest at your body immediately?	-2	-1	**0**	1	2
02) hold head steady without support when looking around?	-2	-1	**0**	1	2
03) hold head steady while you bounce up and down	-2	-1	**0**	1	2
04) hold head steady while you walk or bend down	-2	-1	**0**	1	2
When lying on his/her tummy, your child will					
05) lift head slightly up from the ground and turn head to one side	-2	-1	**0**	1	2
06) lift head fully off the ground by pushing on his/her forearms	-2	-1	**0**	1	2
07) roll over to be on his/her back	-2	-1	**0**	1	2
When lying on his/her back, your child will					
08) move arms and legs vigorously (kicking and reaching movements)	-2	-1	**0**	1	2
09) hold on to your hands and pull herself/himself up to a sit without help	-2	-1	**0**	1	2
10) roll over to be on tummy	-2	-1	**0**	1	2
11) roll over to one side and push up into a crawling position	-2	-1	**0**	1	2
12) get up into a standing position by rolling to a side without help or aids	-2	-1	**0**	1	2
13) stand up without rolling to a side by sitting up and then moving forward	-2	-1	**0**	1	2
When sitting on your lap with back support provided by you, your child will					
14) hold his/her head up and steady when looking around the room	-2	-1	**0**	1	2
When placed into a crawling position resting on hands and knees, your child will					
15) shift weight to one arm and extend the other to reach, wave, or point	-2	-1	**0**	1	2
16) lift up bottom and remain in this position for a short time?	-2	-1	**0**	1	2
17) crawl forward for a few steps (3-5)?	-2	-1	**0**	1	2
When placed into a sitting position on the floor, your child is able to					
18) sit independently without support (hands lifted up)	-2	-1	**0**	1	2
19) use hands and legs to scoot forward on his/her bottom?	-2	-1	**0**	1	2
20) maintain a stable sitting position while turning head and torso to look around?	-2	-1	**0**	1	2
21) hold on to some furniture and pull into a standing position	-2	-1	**0**	1	2
22) shift into a crawling position and try to crawl forward	-2	-1	**0**	1	2

When placed into a standing position, your child will					
23) bounce up and down slightly while holding on to you with both hands	-2	-1	**0**	1	2
24) take a few (wobbly) steps while holding on to you with one hand	-2	-1	**0**	1	2
25) stand alone for a few seconds without help	-2	-1	**0**	1	2
26) walk 4 or 5 steps independently with arms raised	-2	-1	**0**	1	2
27) is able to stand and toss a ball at the same time without loosing balance and falling over	-2	-1	**0**	1	2
28) squat down to pick up a toy from the ground	-2	-1	**0**	1	2
When placed in front of a flight of stairs, your child is able to					
29) creep up the stairs independently?	-2	-1	**0**	1	2
30) walk up stairs (4-5 steps) with both hands held by a caregiver?	-2	-1	**0**	1	2
31) walk up stairs (4-5 steps) with one hand held by a caregiver?	-2	-1	**0**	1	2
32) walk up stairs alone while holding onto a wall or railing?	-2	-1	**0**	1	2
33) walk up stairs without aid? (4 or more steps)	-2	-1	**0**	1	2
34) creep down the stairs independently (feet first)?	-2	-1	**0**	1	2
35) walk down stairs without aid or help?	-2	-1	**0**	1	2
When moving around freely, your child will					
36) run short distances around the room	-2	-1	**0**	1	2
37) run around the room making turns and stops without falling	-2	-1	**0**	1	2
38) kick a ball or small toy forward with one of his/her feet	-2	-1	**0**	1	2
39) stand on one foot when holding your hand (e.g., during dancing)	-2	-1	**0**	1	2
40) demonstrate walking on toes for a short time	-2	-1	**0**	1	2
41) jump in place with both feet up in the air (e.g., during dancing)	-2	-1	**0**	1	2
42) hop in place while balancing on one foot	-2	-1	**0**	1	2
43) jump down from boxes, small steps, or similar without falling	-2	-1	**0**	1	2
When walking down a hallway or small room, your child will					
44) walk in a straight line for a few (4-5) steps with arms up	-2	-1	**0**	1	2
45) walk in a straight path without bumping into the walls using arms to balance	-2	-1	**0**	1	2
46) walk in a straight line with arms lowered and swinging freely	-2	-1	**0**	1	2
During free play or pretend play, you notice your child is able to					
47) walk backwards for several (5 or more) steps?	-2	-1	**0**	1	2
48) jump forward over small obstacles such as a curb or box?	-2	-1	**0**	1	2
49) purposefully do a somersault?	-2	-1	**0**	1	2

Section 2: Fine motor skills

(48 items)

In the following please think about your child's fine motor skills such as reaching, grasping, orienting, and drawing. How easily can your child manipulate small objects and coordinate his/her hands?

→ Skills are organized by posture and increase in difficulty within each posture.

While observing your child lying on his/her back in a crib, baby gym, or on the floor, you notice your child					
01) holding his/her hands close to the body in little fists occasionally?	-2	-1	**0**	1	2
02) tightly holding on to a toy placed into his/her hand?	-2	-1	**0**	1	2
03) bringing both hands together near the face, chest, or tummy?	-2	-1	**0**	1	2
04) opening up the fingers of each hand spontaneously?	-2	-1	**0**	1	2
05) spontaneously bringing one hand up to the mouth?	-2	-1	**0**	1	2
06) pulling on a string to obtain an object beyond reach?	-2	-1	**0**	1	2
When sitting on your lap or in a high chair while playing with toys, you notice your child is able to					
07) successfully hold on to a small object such as a ring or stick?	-2	-1	**0**	1	2
08) reach for a toy with one hand by extending the arm and fingers?	-2	-1	**0**	1	2
09) successfully grasp a toy with one hand following a reach?	-2	-1	**0**	1	2
10) transfer toys from one hand to the other hand?	-2	-1	**0**	1	2
11) purposefully bang toys on the table or tray?	-2	-1	**0**	1	2
12) purposefully drop toys or throw them off the table?	-2	-1	**0**	1	2
13) manipulate one toy with both hands simultaneously?	-2	-1	**0**	1	2
14) place beads on a string without help?	-2	-1	**0**	1	2
When sitting without support on the floor or in a small chair, you notice your child					
15) shaking small toys such as a rattle without loosing balance?	-2	-1	**0**	1	2
16) picking up small objects (e.g., cheerios) using index finger and thumb?	-2	-1	**0**	1	2
17) holding one toy in each hand and banging them together?	-2	-1	**0**	1	2
18) taking toys out of a box, bucket, or container?	-2	-1	**0**	1	2
19) putting toys into a box, bucket, or container?	-2	-1	**0**	1	2
20) stacking 3 or more blocks vertically?	-2	-1	**0**	1	2
When playing with a book or magazine, most of the time your child will					
21) turn several pages at the same time?	-2	-1	**0**	1	2
22) turn one page at a time?	-2	-1	**0**	1	2

When drawing on a sheet of paper using a crayon or pen, your child will					
23) grip the crayon with a fist?	-2	-1	**0**	1	2
24) grip the crayon with thumb and index finger (right side down)?	-2	-1	**0**	1	2
25) make a mark on the paper in any direction?	-2	-1	**0**	1	2
26) mark vertical lines on the paper?	-2	-1	**0**	1	2
27) mark horizontal lines on the paper?	-2	-1	**0**	1	2
28) copy and reproduce simple drawings (e.g., circle) by a caregiver?	-2	-1	**0**	1	2
29) copy and reproduce multi-stroke drawings (e.g., square)?	-2	-1	**0**	1	2
30) copy and reproduce complex drawings (e.g., letters, triangle, cross)?	-2	-1	**0**	1	2
31) draw letters the right way round and proportional in size?	-2	-1	**0**	1	2
When playing with a sheet of paper, your child can do the following with the paper					
32) grasp the paper and pull or wrinkle it?	-2	-1	**0**	1	2
33) roll the paper in a tube shape?	-2	-1	**0**	1	2
34) fold the paper three times (any way)?	-2	-1	**0**	1	2
35) fold the paper in half two times to form a square?	-2	-1	**0**	1	2
When playing with a shape sorter or piggy bank, you notice your child					
36) is able to successfully place circular shapes into the sorter?	-2	-1	**0**	1	2
37) is able to place complex shapes (e.g., triangle) into the sorter?	-2	-1	**0**	1	2
38) rotates and successfully inserts small objects (e.g., coins)?	-2	-1	**0**	1	2
When playing with building blocks, you notice your child will					
39) stack block towers of 6 blocks or more?	-2	-1	**0**	1	2
40) add a block to a tall tower without knocking it over?	-2	-1	**0**	1	2
41) copy you or other children by building a similar tower?	-2	-1	**0**	1	2
When playing with activity books or color books, your child occasionally will					
42) fill in color areas while staying inside the object's boundaries?	-2	-1	**0**	1	2
43) connect lines in a maze or draw by numbers game?	-2	-1	**0**	1	2
When getting dressed or undressed, your child sometimes is able to					
44) open shoelaces by pulling?	-2	-1	**0**	1	2
45) open Velcro latches by pulling?	-2	-1	**0**	1	2
46) open zippers by pulling?	-2	-1	**0**	1	2
47) open buttons?	-2	-1	**0**	1	2
48) close a zipper or buttons by himself/herself?	-2	-1	**0**	1	2

Section 3: Perception Action

(31 items)

In the following please think about your child's visual and receptive skills. Can your child make out small details on pictures? Does your child orient to sounds and respond to stimulation easily?

→ Skills are organized by posture and increase in difficulty within each posture.

While lying on his/her back in a crib, baby gym, or on the floor, your child sometimes will					
01) fixate on objects that are moved close to your child's eyes?	-2	-1	0	1	2
02) turn the head all the way to one side (90°) to follow your face?	-2	-1	0	1	2
03) notice his/her own hands and look at them for some time?	-2	-1	0	1	2
04) swat at toys hanging from a baby gym or car seat?	-2	-1	0	1	2
While sitting on your lap or fully supported in a high chair or car seat, you have noticed your child					
05) follow a person or object by turning his/her head slightly?	-2	-1	0	1	2
06) turn the head from side to side (180°) to follow something interesting?	-2	-1	0	1	2
07) shift eye gaze back and forth between your face and an object?	-2	-1	0	1	2
08) focus on a far away object (e.g., toy across the room)?	-2	-1	0	1	2
09) orient to noises and visually search for the cause of the noise?	-2	-1	0	1	2
10) extend his/her arms towards an object that is close by?	-2	-1	0	1	2
11) pull on a string or cloth to obtain a connected object?	-2	-1	0	1	2
When your child is sitting on the floor on his/her own without support, your child will					
12) pull an object to reveal another object that was hidden underneath?	-2	-1	0	1	2
13) find a hidden object when given multiple choices to search?	-2	-1	0	1	2
14) turn cups right side up during play?	-2	-1	0	1	2
15) sometimes use objects functionally and appropriately on him/herself (e.g., comb own hair with comb, eat with spoon)?	-2	-1	0	1	2
16) sometimes use objects functionally and appropriately on others (e.g., comb your hair, feed puppet)?	-2	-1	0	1	2
When playing with your child sitting at a table or in a high chair with tray attached, your child will					
17) open and close a book using two hands?	-2	-1	0	1	2
18) touch pictures in a book and vocalize about them?	-2	-1	0	1	2
19) turn cups right side up during play?	-2	-1	0	1	2
20) nest 2 or 3 nesting cups or containers by putting one inside another?	-2	-1	0	1	2
21) nest 4 or more nesting cups or toys correctly?	-2	-1	0	1	2
When playing with a wooden puzzle or form board, you child is able to					
22) insert simple, rounded shapes correctly into the puzzle?	-2	-1	0	1	2
23) insert shapes with edges (e.g., triangle) correctly into the puzzle?	-2	-1	0	1	2

When being asked to find or show an item, your child is able to					
24) find items of pairs (e.g., where is the other shoe, sock, glove)?	-2	-1	**0**	1	2
25) find identical items (e.g., this is your spoon, where is my spoon)?	-2	-1	**0**	1	2
26) match pictures in a picture book (e.g., where is the other dog)?	-2	-1	**0**	1	2
27) match letters (e.g., pointing out same letters)?	-2	-1	**0**	1	2
When cleaning up after play or sorting during play, your child can when asked to					
28) sort toys by category (e.g., blocks in one box, puppets in another)?	-2	-1	**0**	1	2
29) sort toys by shape, size, or color?	-2	-1	**0**	1	2
When reading a book or looking at a picture in a newspaper or photo book, your child will					
30) point to the same item or person across multiple pictures?	-2	-1	**0**	1	2
31) look to where you point?	-2	-1	**0**	1	2

Appendix F

Walking and Crawling Onset

Based on memory or with the assistance of diary, photo, or video records please recall the following information to the best of your ability. Answer DNR if you do not remember

a)At what age was your child able to crawl?
_____ _____ months

b)How did you estimate when your child began to crawl unaided?
○ memory ○ diary, instagram/facebook, or other calendar record
○ dated video or picture

c)At what age was your child able to independently walk unaided?
_____ _____ months

d)How did you estimate when your child began to walk unaided?
○ memory ○ diary, instagram/facebook, or other calendar record
○ dated video or picture

Appendix G

Supplemental Tables

Supplemental Table 1. Difference in Maternal Characteristics Between Responders and Non-Responders

Mean (SD)	Parent Study (103)	Non-responders (31)	p-value
Age, years	31.3 (4.7)	29.6 (5.3)	0.015
Pre-pregnancy BMI, kg/m^2	26.1 (6.6)	26.0 (6.3)	0.927
n (%)			
Sedentary Trajectory			0.798
Low	20 (19)	7 (23)	
Medium	41 (40)	11 (35)	
High	42 (41)	13 (42)	
MVPA Trajectory			0.665
Low	25 (24)	7 (23)	
Medium	54 (52)	15 (48)	
High	24 (23)	9 (29)	
Maternal Education			<0.001
Highschool or less	8 (8)	7 (23)	
Some college or training	21 (20)	10 (32)	
College grad	27 (26)	6 (19)	
Masters/Doctoral	47 (46)	8 (26)	
Race			
White	81 (79)	20 (65)	0.008
Black	16 (15)	10 (32)	
Other	6 (6)	1 (3)	

BMI: Body Mass Index

p-value represents difference between responders and non-responders from parent study recruitment

Supplemental Table 2. Participant Characteristics Among Those With and Without Catch-Up Growth (n=60)

	Catch-up Growth		
Mean (SD)	No (46)	Yes (14)	p-value
Age, months	20.7 (5.1)	22.1 (5.0)	0.360
Gestational age at birth, weeks	39.3 (1.3)	37.9 (2.0)	**0.004**
Maternal Pre-pregnancy BMI, kg/m^2	26.5 (7.2)	23.7 (4.1)	0.179
Maternal EPDS score*	3.0 (3.0)	4.7 (4.1)	0.156
n (%)			
Sex			0.451
Male	25 (54)	6 (43)	
Female	21 (46)	8 (57)	
Feeding type			1.000
Exclusively breastfed	23 (50)	7 (50)	
Partial breastfeeding	21 (46)	6 (43)	
Exclusively formula fed	2 (4)	1 (7)	
Maternal Education			0.144
Some college or training	9 (20)	0	
College grad	9 (20)	2 (14)	
Masters/Doctoral	28 (60)	12 (86)	
Household Income			1.000
<50,000	4 (9)	1 (7)	
50-<75,000	5 (11)	1 (7)	
>75,000	35 (76)	12 (86)	
Don't know/refused	2 (4)	0	
Race			0.196
White	35 (76)	14 (100)	
Black	6 (13)	0	
Other	5 (11)	0	

EPDS: Edinburgh Postpartum Depression Score, BMI: Body Mass Index
*Fewer observations available for EPDS score (n=35, n=9)

Supplemental Table 3. Associations of EMQ Score Domains With Covariates

	Gross motor		Fine motor		Perception action	
	r	p-value	r	p-value	r	p-value
Gestational age at birth, weeks	0.075	0.540	0.028	0.823	-0.012	0.924
Maternal Pre-pregnancy BMI, kg/m^2	**0.253**	**0.037**	-0.023	0.850	-0.179	0.144
Maternal EPDS score*	**-0.302**	**0.044**	-0.279	0.064	-0.251	0.096
	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
Sex		0.967		0.947		0.496
Male	72.7 (13.6)		38.9 (12.7)		48.2 (19.2)	
Female	71.9 (13.7)		38.0 (12.9)		46.0 (9.4)	
Feeding type		0.809		0.952		0.376
Exclusively breastfed	72.8 (13.6)		38.7 (12.7)		48.2 (9.0)	
Partial breastfeeding	72.0 (13.9)		38.7 (13.0)		46.8 (9.5)	
Exclusively formula fed	69.0 (12.7)		33.3 (12.0)		36.7 (9.5)	
Maternal Education		0.193		0.592		0.512
Some college or training	79.4 (13.0)		36.3 (12.3)		43.0 (8.8)	
College grad	74.6 (13.7)		43.4 (12.9)		46.8 (9.9)	
Masters/Doctoral	68.9 (13.6)		36.6 (12.8)		48.3 (9.5)	
Household Income		0.567		0.348		0.091
<50,000	74.8 (14.8)		42.5 (13.7)		44.2 (9.7)	
50-<75,000	74.9 (14.9)		37.2 (13.7)		40.4 (9.5)	
>75,000	71.3 (13.9)		38.6 (13.3)		48.9 (6.8)	
Don't know/refused	78.3 (10.4)		32.0 (10.0)		39.7 (6.8)	
Race		0.418		0.988		**0.034**
White	72.2 (13.7)		39.5 (12.5)		49.1 (8.7)	
Black	74.2 (11.7)		33.7 (10.7)		33.2 (7.1)	
Other	70.5 (17.9)		33.3 (16.4)		42.3 (10.9)	

Partial correlations with continuous covariates represent the association between variables while holding age constant

Predicted mean score by categorical covariates generated using ANCOVA adjusted for age splines

*Fewer observations available for EPDS score (n=47)

Supplemental Table 4 Predicted EMQ Scores by Activity Trajectory

		Sedentary Trajectory		MVPA trajectory	
EMQ Domain		Predicted Mean	95% CI	Predicted Mean	95% CI
Gross Motor	Low	75.19	66.67, 83.72	70.71	63.82, 77.59
	Medium	71.46	66.03, 76.88	71.02	66.29, 75.75
	High	71.09	65.66, 76.52	76.03	68.29, 83.78
Fine Motor	Low	42.72	33.84, 51.60	29.45	22.63, 36.27
	Medium	37.85	32.20, 43.50	40.45	35.76, 45.13
	High	36.61	30.95, 42.28	43.21	35.53, 50.89
Perception Action	Low	49.41	41.98, 55.85	41.20	36.21, 46.20
	Medium	47.60	43.50, 51.69	48.23	44.80, 51.65
	High	45.23	41.13, 49.33	50.77	45.15, 56.39

Bibliography

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation.* 2019;139(10):e56-e528.

2. WHO. *Global status report on noncommunicable diseases 2014.* World Health Organization;2014.

3. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. In: Oxford University Press; 2002.

4. Eriksson JG. Developmental Origins of Health and Disease – from a small body size at birth to epigenetics. *Annals of Medicine.* 2016;48(6):456-467.

5. Gluckman PD, Buklijas T, Hanson MA. The developmental origins of health and disease (DOHaD) concept: past, present, and future. In: *The epigenome and developmental origins of health and disease.* Elsevier; 2016:1-15.

6. Bryan S, Hindmarsh P. Normal and abnormal fetal growth. *Hormone Research in Paediatrics.* 2006;65(Suppl. 3):19-27.

7. Godfrey K, Cameron I, Hanson M. Long-term consequences of foetal restriction. *Current Obstetrics & Gynaecology.* 2006;16(5):267-272.

8. Lurbe E, Garcia-Vicent C, Torro MI, Aguilar F, Redon J. Associations of birth weight and postnatal weight gain with cardiometabolic risk parameters at 5 years of age. *Hypertension.* 2014;63(6):1326-1332.

9. Lurbe E, Aguilar F, Álvarez J, Redon P, Torró MI, Redon J. Determinants of cardiometabolic risk factors in the first decade of life: a longitudinal study starting at birth. *Hypertension.* 2018;71(3):437-443.

10. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *Bmj.* 2000;320(7240):967-971.

11. Karaolis-Danckert N, Buyken AE, Bolzenius K, Perim de Faria C, Lentze MJ, Kroke A. Rapid growth among term children whose birth weight was appropriate for gestational age has a longer lasting effect on body fat percentage than on body mass index. *The American Journal of Clinical Nutrition.* 2006;84(6):1449-1455.

12. Eriksson J, Forsen T, Tuomilehto J, Jaddoe V, Osmond C, Barker D. Effects of size at birth and childhood growth on the insulin resistance syndrome in elderly individuals. *Diabetologia.* 2002;45(3):342-348.

13. Barker DJ, Osmond C, Golding J, Kuh D, Wadsworth ME. Growth in utero, blood pressure in childhood and adult life, and mortality from cardiovascular disease. *BMJ (Clinical research ed).* 1989;298(6673):564-567.

14. Barker DJ. Fetal origins of coronary heart disease. *Bmj.* 1995;311(6998):171-174.

15. Barker DJ. In utero programming of chronic disease. *Clinical science.* 1998;95(2):115-128.

16. Barker DJ. The origins of the developmental origins theory. *Journal of internal medicine.* 2007;261(5):412-417.

17. Dimasuay KG, Boeuf P, Powell TL, Jansson T. Placental Responses to Changes in the Maternal Environment Determine Fetal Growth. *Frontiers in Physiology.* 2016;7(12).

18. Barakat R, Cordero Y, Coteron J, Luaces M, Montejo R. Exercise during pregnancy improves maternal glucose screen at 24–28 weeks: a randomised controlled trial. *Br J Sports Med.* 2012;46(9):656-661.

19. Brett K, Ferraro Z, Holcik M, Adamo K. Prenatal physical activity and diet composition affect the expression of nutrient transporters and mTOR signaling molecules in the human placenta. *Placenta.* 2015;36(2):204-212.

20. da Silva SG, Ricardo LI, Evenson KR, Hallal PC. Leisure-Time Physical Activity in Pregnancy and Maternal-Child Health: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Cohort Studies. *Sports Medicine.* 2017;47(2):295-317.

21. Davenport M, Meah V, Ruchat S, et al. Impact of prenatal exercise on neonatal and childhood outcomes: a systematic review and meta-analysis. *British journal of sports medicine.* 2018;52(21):1386.

22. Leet T, Flick L. Effect of exercise on birthweight. *Clinical obstetrics and gynecology.* 2003;46(2):423-431.

23. Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, González-García A, Sánchez-López M, Martínez-Vizcaíno V. Effects of exercise-based interventions on neonatal outcomes: a meta-analysis of randomized controlled trials. *American Journal of Health Promotion.* 2015:ajhp. 140718-LIT-140351.

24. Wiebe HW, Boule NG, Chari R, Davenport MH. The effect of supervised prenatal exercise on fetal growth: a meta-analysis. *Obstet Gynecol.* 2015;125(5):1185-1194.

25. Álvarez-Bueno C, Cavero-Redondo I, Sánchez-López M, Garrido-Miguel M, Martínez-Hortelano JA, Martínez-Vizcaíno V. Pregnancy leisure physical activity and children's

neurodevelopment: a narrative review. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2018;125(10):1235-1242.

26. Barnes J, Behrens TK, Benden ME, et al. Letter to the Editor: Standardized use of the terms" sedentary" and" sedentary behaviours". *Applied Physiology Nutrition and Metabolism-Physiologie Appliquee Nutrition Et Metabolisme.* 2012;37(3):540-542.

27. Takito MY, Benício MHDA. Physical activity during pregnancy and fetal outcomes: a case-control study. *Revista de saude publica.* 2010;44(1):90-101.

28. Badon SE, Littman AJ, Chan KG, Williams MA, Enquobahrie DA. Maternal sedentary behavior during pre-pregnancy and early pregnancy and mean offspring birth size: a cohort study. *BMC pregnancy and childbirth.* 2018;18(1):267.

29. Ruifrok AE, Althuizen E, Oostdam N, et al. The relationship of objectively measured physical activity and sedentary behaviour with gestational weight gain and birth weight. *Journal of pregnancy.* 2014;2014.

30. Baena-García L, Ocón-Hernández O, Acosta-Manzano P, et al. Association of sedentary time and physical activity during pregnancy with maternal and neonatal birth outcomes. The GESTAFIT Project. *Scand J Med Sci Sports.* 2019;29(3):407-414.

31. Zheng M, Lamb KE, Grimes C, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. *Obes Rev.* 2018;19(3):321-332.

32. Singhal A. Long-term adverse effects of early growth acceleration or catch-up growth. *Annals of Nutrition and Metabolism.* 2017;70(3):236-240.

33. Kelishadi R, Haghdoost AA, Jamshidi F, Aliramezany M, Moosazadeh M. Low birthweight or rapid catch-up growth: which is more associated with cardiovascular disease and its risk factors in later life? A systematic review and cryptanalysis. *Paediatrics and international child health.* 2015;35(2):110-123.

34. Woo JG. Infant growth and long-term cardiometabolic health: A review of recent findings. *Current nutrition reports.* 2019;8(1):29-41.

35. Kang MJ. The adiposity rebound in the 21st century children: meaning for what? *Korean J Pediatr.* 2018;61(12):375-380.

36. Barnett LM, Van Beurden E, Morgan PJ, Brooks LO, Beard JR. Childhood motor skill proficiency as a predictor of adolescent physical activity. *Journal of adolescent health.* 2009;44(3):252-259.

37. Graf C, Koch B, Kretschmann-Kandel E, et al. Correlation between BMI, leisure habits and motor abilities in childhood (CHILT-project). *International journal of obesity.* 2004;28(1):22.

38. Gibbs BB, Paley JL, Jones MA, Whitaker KM, Connolly CP, Catov JM. Validity of self-reported and objectively measured sedentary behavior in pregnancy. *BMC pregnancy and childbirth.* 2020;20(1):99.

39. Clapp J. Influence of endurance exercise and diet on human placental development and fetal growth. *Placenta.* 2006;27(6-7):527-534.

40. Dumortier O, Blondeau B, Duvillie B, Reusens B, Breant B, Remacle C. Different mechanisms operating during different critical time-windows reduce rat fetal beta cell mass due to a maternal low-protein or low-energy diet. *Diabetologia.* 2007;50(12):2495-2503.

41. Woods LL, Weeks DA, Rasch R. Programming of adult blood pressure by maternal protein restriction: role of nephrogenesis. *Kidney international.* 2004;65(4):1339-1348.

42. Dodson RB, Rozance PJ, Fleenor BS, et al. Increased arterial stiffness and extracellular matrix reorganization in intrauterine growth–restricted fetal sheep. *Pediatr Res.* 2013;73(2):147.

43. Leitner Y, Fattal-Valevski A, Geva R, et al. Neurodevelopmental outcome of children with intrauterine growth retardation: a longitudinal, 10-year prospective study. *Journal of child neurology.* 2007;22(5):580-587.

44. Jiang B, Godfrey KM, Martyn CN, Gale CR. Birth weight and cardiac structure in children. *Pediatrics.* 2006;117(2):e257-e261.

45. Eriksson JG, Forsen T, Tuomilehto J, Osmond C, Barker DJ. Early growth and coronary heart disease in later life: longitudinal study. *Bmj.* 2001;322(7292):949-953.

46. Claris O, Beltrand J, Levy-Marchal C. Consequences of intrauterine growth and early neonatal catch-up growth. Paper presented at: Seminars in perinatology2010.

47. Whincup P, Kaye S, Owen C, et al. Birth weight and risk of type 2 diabetes: a systematic review. In:2008.

48. Verkauskiene R, Beltrand J, Claris O, et al. Impact of fetal growth restriction on body composition and hormonal status at birth in infants of small and appropriate weight for gestational age. *European journal of endocrinology.* 2007;157(5):605-612.

49. Physical Activity and Exercise During Pregnancy and the Postpartum Period: ACOG Committee Opinion, Number 804. *Obstetrics & Gynecology.* 2020;135(4):e178-e188.

50. Evenson KR, Wen F. Prevalence and correlates of objectively measured physical activity and sedentary behavior among US pregnant women. *Preventive medicine.* 2011;53(1-2):39-43.

51. Sun C, Velazquez MA, Fleming TP. DOHaD and the periconceptional period, a critical window in time. In: *The epigenome and developmental origins of health and disease.* Elsevier; 2016:33-47.

52. Hendrix N, Berghella V. Non-placental causes of intrauterine growth restriction. Paper presented at: Seminars in perinatology2008.

53. Cameron AJ, Spence AC, Laws R, Hesketh KD, Lioret S, Campbell KJ. A review of the relationship between socioeconomic position and the early-life predictors of obesity. *Current obesity reports.* 2015;4(3):350-362.

54. Alhusen JL, Bower KM, Epstein E, Sharps P. Racial discrimination and adverse birth outcomes: an integrative review. *Journal of midwifery & women's health.* 2016;61(6):707-720.

55. Gentner MB, Leppert MLOC. Environmental influences on health and development: nutrition, substance exposure, and adverse childhood experiences. *Developmental Medicine & Child Neurology.* 2019.

56. Barker DJ, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. *Lancet (London, England).* 1986;1(8489):1077-1081.

57. Bertram CE, Hanson MA. Animal models and programming of the metabolic syndrome: Type 2 diabetes. *British Medical Bulletin.* 2001;60(1):103-121.

58. Langley-Evans SC. Metabolic programming in pregnancy: studies in animal models. *Genes & Nutrition.* 2007;2(1):33-38.

59. Fayyaz J. Ponderal index. 2005.

60. Fay RA, Dey PL, Saadie CM, Buhl JA, Gebski VJ. Ponderal index: a better definition of the 'at risk'group with intrauterine growth problems than birth-weight for gestational age in term infants. *Australian and New Zealand journal of obstetrics and gynaecology.* 1991;31(1):17-19.

61. Gaccioli F, Lager S, Powell T, Jansson T. Placental transport in response to altered maternal nutrition. *Journal of developmental origins of health and disease.* 2013;4(2):101-115.

62. Challier J, Basu S, Bintein T, et al. Obesity in pregnancy stimulates macrophage accumulation and inflammation in the placenta. *Placenta.* 2008;29(3):274-281.

63. Pantham P, Aye ILH, Powell TL. Inflammation in maternal obesity and gestational diabetes mellitus. *Placenta.* 2015;36(7):709-715.

64. Schaefer-Graf UM, Kjos SL, Fauzan OH, et al. A randomized trial evaluating a predominately fetal growth–based strategy to guide management of gestational diabetes in Caucasian women. *Diabetes care.* 2004;27(2):297-302.

65. Gluckman PD, Hanson MA, Beedle AS. Early life events and their consequences for later disease: a life history and evolutionary perspective. *American Journal of Human Biology.* 2007;19(1):1-19.

66. Godfrey KM, Lillycrop KA, Burdge GC, Gluckman PD, Hanson MA. Epigenetic mechanisms and the mismatch concept of the developmental origins of health and disease. *Pediatr Res.* 2007;61(5 Part 2):5R.

67. Gluckman P, Hanson M. *Mismatch: Why our world no longer fits our bodies.* Oxford University Press; 2006.

68. Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. *JAMA.* 2018;320(19):2020-2028.

69. Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. *Am J Prev Med.* 2011;41(2):207-215.

70. Di Fabio DR, Blomme CK, Smith KM, Welk GJ, Campbell CG. Adherence to physical activity guidelines in mid-pregnancy does not reduce sedentary time: an observational study. *International Journal of Behavioral Nutrition and Physical Activity.* 2015;12(1):27.

71. Norris T, Johnson W, Farrar D, Tuffnell D, Wright J, Cameron N. Small-for-gestational age and large-for-gestational age thresholds to predict infants at risk of adverse delivery and neonatal outcomes: are current charts adequate? An observational study from the Born in Bradford cohort. *BMJ open.* 2015;5(3):e006743.

72. Pastorino S, Bishop T, Crozier SR, et al. Associations between maternal physical activity in early and late pregnancy and offspring birth size: remote federated individual level meta-analysis from eight cohort studies. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2019;126(4):459-470.

73. Godfrey K. The'developmental origins' hypothesis: Epidemiology. 2006.

74. Gibbs BB, Jones MA, Paley JL, Whitaker KM, Connolly CP, Catov JM. Validity Of Objectively-measured And Self-reported Sedentary Behavior Across Three Trimesters Of Pregnancy: 1367: Board #129 May 30 9:30 AM - 11:00 AM. *Medicine & Science in Sports & Exercise.* 2019;51(6):365.

75. Jones MA, Catov J, Jeyevalan A, Jakicic J, Whitaker K, Gibbs BB. Sedentary Behavior Across Pregnancy, Gestational Age at Delivery, and Birthweight: 1793 May 30 3:45 PM - 4:00 PM. *Medicine & Science in Sports & Exercise.* 2019;51(6S):475-476.

76. Clapp III JF. Morphometric and neurodevelopmental outcome at age five years of the offspring of women who continued to exercise regularly throughout pregnancy. *The Journal of pediatrics.* 1996;129(6):856-863.

77. Chiavaroli V, Hopkins SA, Derraik JG, et al. Exercise in pregnancy: 1-year and 7-year follow-ups of mothers and offspring after a randomized controlled trial. *Scientific reports.* 2018;8(1):1-9.

78. Tanvig M, Vinter CA, Jørgensen JS, et al. Effects of lifestyle intervention in pregnancy and anthropometrics at birth on offspring metabolic profile at 2.8 years: results from the Lifestyle in Pregnancy and Offspring (LiPO) study. *The Journal of Clinical Endocrinology & Metabolism.* 2015;100(1):175-183.

79. Gallahue D, Ozmun J. Understanding motor development: infants, children, adolescents, adults. 2006. *Chapter.*13:267-274.

80. Folio MK FR. Peabody Developmental Motor Scales: Examininer's Manual . 2nd ed. *Austin, Tex: PRO-ED, Inc.* 2000.

81. Bayley N. *Bayley scales of infant development: Manual.* Psychological Corporation; 1993.

82. Bricker D, Squires J, Mounts L, et al. Ages and stages questionnaire. *Paul H Brookes: Baltimore.* 1999.

83. Libertus K, Landa RJ. The Early Motor Questionnaire (EMQ): a parental report measure of early motor development. *Infant Behav Dev.* 2013;36(4):833-842.

84. McMillan AG, May LE, Gaines GG, Isler C, Kuehn D. Effects of Aerobic Exercise during Pregnancy on 1-Month Infant Neuromotor Skills. *Med Sci Sports Exerc.* 2019;51(8):1671-1676.

85. Ellingsen MS, Pettersen A, Stafne SN, Mørkved S, Salvesen KÅ, Evensen KAI. Neurodevelopmental outcome in 7-year-old children is not affected by exercise during pregnancy: follow up of a multicentre randomised controlled trial. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2020;127(4):508-517.

86. Hellenes OM, Vik T, Løhaugen GC, et al. Regular moderate exercise during pregnancy does not have an adverse effect on the neurodevelopment of the child. *Acta Paediatrica.* 2015;104(3):285-291.

87. Eriksson JG, Forsen T, Tuomilehto J, Winter PD, Osmond C, Barker DJ. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. *Bmj.* 1999;318(7181):427-431.

88. Huxley R, Owen CG, Whincup PH, et al. Is birth weight a risk factor for ischemic heart disease in later life? *Am J Clin Nutr.* 2007;85(5):1244-1250.

89. Bloch MJ, FASH F, Basile FJ. Cardiovascular risks of hypertension.

90. Olson M, Chambers M, Shaibi G. Pediatric markers of adult cardiovascular disease. *Current pediatric reviews.* 2017;13(4):255-259.

91. Law C, Shiell A, Newsome C, et al. Fetal, infant, and childhood growth and adult blood pressure: a longitudinal study from birth to 22 years of age. *Circulation.* 2002;105(9):1088-1092.

92. Law CM, Shiell AW. Is blood pressure inversely related to birth weight? The strength of evidence from a systematic review of the literature. *Journal of hypertension.* 1996;14(8):935-941.

93. Skilton MR, Marks GB, Ayer JG, et al. Weight gain in infancy and vascular risk factors in later childhood. *Pediatrics.* 2013;131(6):e1821-e1828.

94. Malik M. Heart rate variability: Standards of measurement, physiological interpretation, and clinical use: Task force of the European Society of Cardiology and the North American Society for Pacing and Electrophysiology. *Annals of Noninvasive Electrocardiology.* 1996;1(2):151-181.

95. Dissanayake H, McMullan R, Kong Y, et al. Body Fatness and Cardiovascular Health in Newborn Infants. *Journal of clinical medicine.* 2018;7(9):270.

96. Galland BC, Taylor BJ, Bolton DP, Sayers RM. Heart rate variability and cardiac reflexes in small for gestational age infants. *Journal of applied physiology.* 2006;100(3):933-939.

97. Organization WH, Unicef. Low birthweight: country, regional and global estimates. 2004.

98. Hediger ML, Overpeck MD, Ruan WJ, Troendle JF. Birthweight and gestational age effects on motor and social development. *Paediatric and perinatal epidemiology.* 2002;16(1):33-46.

99. Lubans DR, Morgan PJ, Cliff DP, Barnett LM, Okely AD. Fundamental Movement Skills in Children and Adolescents. *Sports Medicine.* 2010;40(12):1019-1035.

100. Johnsson IW, Haglund B, Ahlsson F, Gustafsson J. A high birth weight is associated with increased risk of type 2 diabetes and obesity. *Pediatric obesity.* 2015;10(2):77-83.

101. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics.* 2005;115(3):e290-e296.

102. Palatianou M, Simos Y, Andronikou S, Kiortsis D. Long-term metabolic effects of high birth weight: a critical review of the literature. *Hormone and Metabolic Research.* 2014;46(13):911-920.

103. Khambalia AZ, Algert CS, Bowen JR, Collie RJ, Roberts CL. Long-term outcomes for large for gestational age infants born at term. *Journal of paediatrics and child health.* 2017;53(9):876-881.

104. Thornburg KL, Marshall N. The placenta is the center of the chronic disease universe. *American Journal of Obstetrics & Gynecology.* 2015;213(4):S14-S20.

105. Vrijens K, Tsamou M, Madhloum N, Gyselaers W, Nawrot TS. Placental hypoxia-regulating network in relation to birth weight and ponderal index: the ENVIR ON AGE Birth Cohort Study. *Journal of translational medicine.* 2018;16(1):2.

106. Blondeau B, Garofano A, Czernichow P, Breant B. Age-dependent inability of the endocrine pancreas to adapt to pregnancy: a long-term consequence of perinatal malnutrition in the rat. *Endocrinology.* 1999;140(9):4208-4213.

107. Yim HE, Yoo KH. Renin-Angiotensin system-considerations for hypertension and kidney. *Electrolyte & Blood Pressure.* 2008;6(1):42-50.

108. Artiga S, Hinton E. Beyond health care: the role of social determinants in promoting health and health equity. *Health.* 2019;20:10.

109. Barker DJ, Forsén T, Uutela A, Osmond C, Eriksson JG. Size at birth and resilience to effects of poor living conditions in adult life: longitudinal study. *Bmj.* 2001;323(7324):1273.

110. Dubois L, Girard M. Determinants of birthweight inequalities: Population-based study. *Pediatrics International.* 2006;48(5):470-478.

111. Louis GMB, Grewal J, Albert PS, et al. Racial/ethnic standards for fetal growth: the NICHD Fetal Growth Studies. *American journal of obstetrics and gynecology.* 2015;213(4):449. e441-449. e441.

112. Bowers K, Laughon S, Kiely M, Brite J, Chen Z, Zhang C. Gestational diabetes, pre-pregnancy obesity and pregnancy weight gain in relation to excess fetal growth: variations by race/ethnicity. *Diabetologia.* 2013;56(6):1263.

113. Guerrero AD, Mao C, Fuller B, Bridges M, Franke T, Kuo AA. Racial and ethnic disparities in early childhood obesity: growth trajectories in body mass index. *Journal of racial and ethnic health disparities.* 2016;3(1):129-137.

114. Taveras EM, Gillman MW, Kleinman K, Rich-Edwards JW, Rifas-Shiman SL. Racial/ethnic differences in early-life risk factors for childhood obesity. *Pediatrics.* 2010;125(4):686-695.

115. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic disparities in childhood obesity: the role of early life risk factors. *JAMA pediatrics.* 2013;167(8):731-738.

116. Whitaker KM, Wilcox S, Liu J, Blair SN, Pate RR. African American and White women′ s perceptions of weight gain, physical activity, and nutrition during pregnancy. *Midwifery.* 2016;34:211-220.

117. Gaston A, Cramp A. Exercise during pregnancy: a review of patterns and determinants. *Journal of Science and Medicine in Sport.* 2011;14(4):299-305.

118. Proper KI, Cerin E, Owen N. Neighborhood and individual socio-economic variations in the contribution of occupational physical activity to total physical activity. *Journal of Physical Activity and Health.* 2006;3(2):179-190.

119. Gay JL, Buchner DM. Ethnic disparities in objectively measured physical activity may be due to occupational activity. *Preventive medicine.* 2014;63:58-62.

120. Cai C, Vandermeer B, Khurana R, et al. The impact of occupational activities during pregnancy on pregnancy outcomes: a systematic review and metaanalysis. *American Journal of Obstetrics and Gynecology.* 2020;222(3):224-238.

121. Catov JM, Parker CB, Gibbs BB, et al. Patterns of leisure-time physical activity across pregnancy and adverse pregnancy outcomes. *International Journal of Behavioral Nutrition and Physical Activity.* 2018;15(1):68.

122. Hegaard HK, Pedersen BK, Bruun Nielsen B, Damm P. Leisure time physical activity during pregnancy and impact on gestational diabetes mellitus, pre-eclampsia, preterm delivery and birth weight: a review. *Acta obstetricia et gynecologica Scandinavica.* 2007;86(11):1290-1296.

123. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics.* 2009;42(2):377-381.

124. Edwardson CL, Winkler EA, Bodicoat DH, et al. Considerations when using the activPAL monitor in field-based research with adult populations. *Journal of Sport and Health Science.* 2017;6(2):162-178.

125. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Medicine & Science in Sports & Exercise.* 2008;40(1):181-188.

126. Jones BL, Nagin DS. A note on a Stata plugin for estimating group-based trajectory models. *Sociological Methods & Research.* 2013;42(4):608-613.

127. Leroy J. ZSCORE06: Stata module to calculate anthropometric z-scores using the 2006 WHO child growth standards. 2011.

128. Van Wyk L, Boers K, van Wassenaer-Leemhuis A, et al. Post-natal catch-up growth after suspected fetal growth restriction at term. *Frontiers in Endocrinology.* 2019;10:274.

129. Effective Practice Guide. Published 2020. Accessed.

130. Acock AC. *A gentle introduction to Stata.* Stata press; 2008.

131. Newton ER, May L. Adaptation of Maternal-Fetal Physiology to Exercise in Pregnancy: The Basis of Guidelines for Physical Activity in Pregnancy. *Clinical Medicine Insights Women's Health.* 2017;10.

132. Hopkins SA, Cutfield WS. Exercise in pregnancy: weighing up the long-term impact on the next generation. *Exercise and sport sciences reviews.* 2011;39(3):120-127.

133. Polańska K, Muszyński P, Sobala W, Dziewirska E, Merecz-Kot D, Hanke W. Maternal lifestyle during pregnancy and child psychomotor development—Polish Mother and Child Cohort study. *Early human development.* 2015;91(5):317-325.

134. Hinkley T, Crawford D, Salmon J, Okely AD, Hesketh K. Preschool children and physical activity: a review of correlates. *American journal of preventive medicine.* 2008;34(5):435-441. e437.

135. Cools W, De Martelaer K, Samaey C, Andries C. Fundamental movement skill performance of preschool children in relation to family context. *Journal of Sports Sciences.* 2011;29(7):649-660.

136. Barnett LM, Hnatiuk JA, Salmon J, Hesketh KD. Modifiable factors which predict children's gross motor competence: a prospective cohort study. *International journal of behavioral nutrition and physical activity.* 2019;16(1):129.