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LEISURE-TIME PHYSICAL ACTIVITY DURING PREGNANCY AND OFFSPRING SIZE

By

Lanay M. Mudd

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ABSTRACT

LEISURE-TIME PHYSICAL ACTIVITY DURING PREGNANCY AND OFFSPRING SIZE

By

Lanay M. Mudd

The aims of this dissertation were to determine the effect of maternal leisure-time physical activity (LTPA) on offspring size at birth, to determine the separate and combined effect of LTPA during pregnancy and child leisure-time behavior on odds of child obesity, and to determine the reliability of postpartum recall of LTPA during pregnancy.

For Aims One and Two, women enrolled in the Pregnancy Outcomes and Community Health study (1998-2004) were followed up in 2007. Follow-up efforts were extensive for a subcohort and minimal for the remainder, or non–subcohort. This resulted in 596 subcohort and 418 non-subcohort women who delivered at term and provided complete information relative to our aims. Original data collection supplied demographic, pregnancy, and birth information. Sex and gestational age specific birth weight z-scores (BWz) were calculated and offspring were categorized as small-, appropriate-, or large-for-gestational-age (SGA, AGA, and LGA, respectively). At follow-up, women recalled pregnancy LTPA and were classified as inactive, insufficiently active, or meeting LTPA recommendations. Women also reported child leisure-time behavior (mostly sedentary, some sedentary/some active, or mostly active) and child height and weight. Children were classified as healthy weight (5-<85^{th}), overweight (85-<95^{th}), or obese (≥95^{th}) based on sex and age specific BMI percentiles.

Among the non-subcohort, meeting LTPA recommendations significantly decreased odds of LGA (aOR=0.30, 95%CI: 0.14-0.64) without affecting odds of SGA. In quantile regression analyses, meeting LTPA recommendations was unrelated to BWz until the 0.65 quantile, after which it significantly reduced BWz. Results for the subcohort were similar but non-significant. Thus, LTPA during pregnancy may benefit maternal/child health by reducing BWz only among the upper parts of the distribution.

Insufficient activity and meeting LTPA recommendations during pregnancy were each associated with borderline significant reduced odds of child obesity by ~50% within the non-subcohort and by~30% within the subcohort. The highest odds of obesity was associated with maternal inactivity during pregnancy combined with sedentary child activity within both the non-subcohort (aOR=2.47, 95%CI: 0.83-7.39) and subcohort (aOR=1.76, 95%CI: 0.84-3.71). Both LTPA during pregnancy and children's own leisure-time behavior appear to contribute towards risk of child obesity.

For Aim Three, 298 women enrolled in the Michigan Alliance for the National Children's Study Pilot Study reported min/wk spent in moderate and vigorous LTPA at their first prenatal care visit (total min/wk of LTPA calculated). At 15-30 months postpartum, 82 women recalled LTPA during the trimester of their original interview. Recalled vigorous (r_s=0.34, p=0.002) and total (r_s=0.28, p=0.016) LTPA values were significantly correlated with original reports, but this was not true for moderate LTPA (r_s=0.10, p=0.350). There was high percent agreement for original vs. recalled report of any moderate, vigorous, or total LTPA (70-79%), but kappa values were low (0.02-0.18). Postpartum recall of LTPA during pregnancy appears to be moderately reliable.

ACKNOWLEDGMENTS

I'd like to acknowledge the many people who helped me complete this work. To all my friends in HERL, thank you for your laughter, stories and support. To the ladies of POUCH, thanks for jumping in at the end and helping me to finish it off by freely sharing all your expertise. To all my helpers with PAPOS, thanks for your hard work and energy as you collected data and helped me explore new research questions with it. I'd like to specifically thank Josh Ode, Jeremy Knous, Patti Bauer, and Sarah Nechuta for all their friendship and advice that helped me get through this entire process. Also thanks to my family who always encouraged me to pursue my dreams. And finally last, but not least, to my advisor and committee members, thanks for inspiring me to formulate and test new questions, to carefully consider the results, and to find the public significance in the work that I do. I have enjoyed the journey to the fullest and look forward to life-long collaborations.

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CHAPTER ONE: INTRODUCTION

Giving birth to an infant that is either too small or too large is associated with adverse health outcomes for both the mother and her child. While the causes and health risks of small infants have received considerable attention, few researchers have examined the etiology of excess fetal growth leading to large birth size. In addition to having an increased risk of birth trauma, it appears that large infants are predisposed towards becoming overweight children.[1, 2] Thus, examining modifiable factors that influence birth size may uncover new pathways for preventing childhood obesity.

Past research among select samples of women has shown that maternal leisure-time physical activity (LTPA) during pregnancy decreases birth size modestly,[3] and reduces the risk of being born large for gestational age.[4] However, the independent effects of pre-pregnancy LTPA, trimester-specific LTPA, and maternal body size on the distribution of offspring birth size are not easy to delineate. In addition, only a couple of small studies have evaluated the relationship between maternal LTPA and offspring size during toddlerhood/childhood.[5] Gaining more insight into the effect of maternal LTPA on birth size could inform future research concerning LTPA recommendations for women of childbearing age. Furthermore, understanding the role of maternal LTPA on offspring growth may also help to formulate new approaches for preventing childhood overweight and obesity.

Finally, the reliability of recalling pregnancy-related LTPA needs to be established in order to facilitate future epidemiological research on the long-term effects of LTPA during pregnancy on maternal and child health outcomes. To date, only one small study has examined the validity of recalling LTPA performed during pregnancy at

6 years postpartum.[6] Using a sample of white, upper-middle class women with mainly high levels of LTPA measured during pregnancy, Bauer et al. found moderate to high agreement between originally measured and recalled amounts of LTPA. However, LTPA had been measured precisely via accelerometry, heart rate telemetry, and LTPA surveys at two time-points during pregnancy among these women.[6] Thus, their ability to recall LTPA may have been influenced by greater attention to their activity during pregnancy. More research is needed to determine whether women with more diverse personal characteristics and/or LTPA participation may have similarly high recall abilities and whether participant characteristics may influence recall ability.

This dissertation evaluates the effects of maternal LTPA during pregnancy on offspring size at birth and in childhood. Additionally, the reliability of pregnancy-related LTPA recalled at two years postpartum is evaluated. Data from the Pregnancy Outcomes and Community Health (POUCH) Study were used to determine relationships among LTPA during pregnancy and offspring size. Women enrolled in the POUCH study were contacted at 3-9 yrs postpartum and asked to recall type, frequency, and duration of up to two leisure-time physical activities they performed most often during a typical week in their POUCH pregnancy. They also reported their children's current height and weight at that time. Previously collected data provided birth weight, gestational age at delivery, and descriptive characteristics.

Women enrolled in the Michigan Alliance for the National Children's Study (MANCS) pilot study were followed-up to assess reliability of recalled LTPA. Women originally reported participation in moderate and vigorous LTPA while pregnant in the summer of 2006. These women were contacted in fall of 2008 to recall their pre-

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pregnancy and trimester specific LTPA using the Modified Activity Questionnaire via a mailed survey or internet survey.[7] Using data from these two cohorts, this dissertation addresses the following three Specific Aims.

RESEARCH AIMS:

Specific Aim 1: To evaluate the effect of LTPA during pregnancy on offspring size at birth, measured continuously as birth weight z-score and categorically as size for gestational age (i.e., small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA)).

H 1.1. We hypothesize that meeting LTPA recommendations during pregnancy will not be associated with a mean change in birth weight z-score in linear regression analyses.

H 1.2. We hypothesize that meeting LTPA recommendations during pregnancy will reduce odds of delivering an LGA infant, without affecting the odds of delivering SGA in logistic regression analyses.

H 1.3. We hypothesize that meeting LTPA recommendations during pregnancy will be associated with lower birth weight z-score only among the upper quantiles of the birth weight z-score distribution in quantile regression analyses.

Specific Aim 2: To determine the separate and combined effect of maternal participation in LTPA during pregnancy and child leisure-time behavior on odds of childhood overweight (body mass index (BMI) $\geq 85^{th}$ to $<95^{th}$ age and sex-specific percentile) and obese (BMI $\geq 95^{th}$ age and sex-specific percentile) status. To assess the interactive effect, a four-category combined variable will be created: inactivity during pregnancy and sedentary child activity (-/-), inactivity during pregnancy and non-sedentary child activity

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(-/+), any LTPA during pregnancy and sedentary child activity (+/-), and any LTPA during pregnancy and non-sedentary child activity (+/+).

H 2.1. We hypothesize that meeting LTPA recommendations during pregnancy will reduce the odds of child overweight and obese status when compared to inactivity during pregnancy.

H 2.2. We hypothesize that more active child leisure-time behavior will be have reduce the odds of child overweight and obese status when compared to sedentary leisure-time behavior.

H 2.3. We hypothesize that inactivity during pregnancy combined with sedentary child activity (-/-) will be associated with the highest odds of child overweight and obese status when compared to the +/+ condition.

Specific Aim 3: To determine the reliability of recalling LTPA during pregnancy at approximately two years postpartum among a diverse sample of women and examine whether participant characteristics are associated with recall ability.

H 3.1. We hypothesize that moderate to strong correlations (i.e., r-values $\geq$0.4) will exist between originally reported and recalled moderate, vigorous and total LTPA.

H 3.2. We hypothesize that strong kappa values (i.e., $\geq$0.8) will indicate good categorical agreement such that women will fall into similar categories of "none vs. any" LTPA and "meeting vs. not meeting" LTPA recommendations when using original and recalled reports of LTPA.

H 3.3. Examining the influences of participant characteristics on recall ability is a descriptive aim, thus we have no hypothesis for the direction of effect. We will

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create strata of women based on descriptive characteristics and compare correlation coefficients for original and recalled moderate, vigorous and total LTPA across strata to assess this portion of Aim Three.

ORGANIZATION OF THE DISSERTATION

This dissertation is divided into two parts, the first focusing on offspring size at birth and the second on child body size and reliability of LTPA recall. Both parts consist of a review of relevant literature followed by a paper(s) that evaluate the Specific Aims. Each paper is in manuscript form (abstract, introduction, methods, results, discussion, and references). The final chapter provides an overall summary of all results and discusses the direction of future research.

Chapters Two and Three evaluate the effects of maternal LTPA on offspring birth size, measured as birth weight z-scores and categorical appropriateness of size for gestational age. Chapter Two is a literature review that introduces common terminology applied to birth size, reviews the epidemiology of large infants, and explores factors known to be related to birth size. It focuses primarily on the influences of maternal size and maternal LTPA on offspring birth size, while highlighting gaps in our current knowledge related to these topics. Chapter Three evaluates the effects of LTPA during pregnancy on the distribution of size at birth using linear, polytomous logistic, and quantile regression analyses (Specific Aim One).

Chapters Four and Five consider the relationships among maternal LTPA during pregnancy, child LTPA, and child body size. Chapter Four is a literature review that introduces the epidemiology of overweight status during toddlerhood and the stability of the relationship between size at birth and toddlerhood. It also discusses the available

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literature linking maternal LTPA during pregnancy to offspring size in childhood. Chapter Five evaluates whether maternal LTPA during pregnancy combined with child LTPA level (measured as sedentary vs. non-sedentary activity choice) protects children from being classified as overweight or obese while controlling for possible confounding factors (Specific Aim Two). The reliability of recalled LTPA during pregnancy at two years postpartum is addressed in Chapter Six (Specific Aim Three).

Finally, Chapter Seven provides an overall summary of results and offers suggestions for future research. The research questions addressed by this dissertation represent important steps in evaluating the role of maternal LTPA participation during pregnancy on offspring growth and development. Results of this study will inform future research on LTPA interventions among pregnant women and will aid childhood obesity prevention efforts.

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CHAPTER TWO

REVIEW OF LITERATURE PART ONE: BIRTH SIZE

INTRODUCTION

While several factors are known to be associated with birth size, causal mechanisms for giving birth to an infant either too small or too large have yet to be fully established. The etiology and health risks of being born small have received considerable attention; however, few researchers have focused on excess fetal growth. Fetal overgrowth leading to large birth size is associated with increased risk of adverse birth outcomes and future childhood overweight status.[1-4] Thus, gaining more insight on potentially modifiable determinants of birth size could improve both short- and long-term health outcomes.

Both pre-pregnancy body size and gestational weight gain are positively related to infant birth size, with the largest infants born to overweight/obese women who gain excess weight during pregnancy.[5, 6] Recent evidence suggests that LTPA during pregnancy may help control excess size at birth[7, 8] and decrease the risk of overfatness during childhood.[9] However, these results were based on small, non-representative samples of women. . Further investigation of the relationships among maternal size and weight gain, LTPA during pregnancy, birth size, and child body size has the potential to elucidate a practical intervention to promote healthy pregnancies, birth outcomes, and child weight status.

TERMINOLOGY

Before examining factors associated with birth size, some terminology must be established. Unadjusted birth weight is used to describe birth size in the crudest form.

While a standard definition exists for low birth weight (birth weight < 2.5 kg), multiple definitions exist for high birth weight or macrosomia (birth weight > 4.0, 4.2, or 4.5 kg).[10-14] Since birth weight is irrevocably tied to the length of gestation, adjusting birth weight for gestational age provides a more precise description of the appropriateness of birth size. Birth weight is often compared to a population standard for the gestational age of the infant and categories are used to define infants born SGA (birth weight < the 10th percentile), AGA (birth weight between the 10th -< 90th percentile), and LGA (birth weight > the 90th or 95th percentile).[15, 16] Once again, differing cut-points have been used to designate LGA infants. Within U.S. populations, the most commonly accepted cut-point for LGA is the 90th percentile; however, some authors have argued for more stringent definitions (>2 standard deviations above mean birth weight), especially among diabetic pregnancies.[12, 16] Previous literature mainly used absolute terms to express birth size (e.g. low birth weight or macrosomia), while more recent literature has preferred using relative measures (e.g. SGA or LGA) to describe size at birth.

Using either absolute or relative cut-points to designate in/appropriate birth size is useful for calculating and interpreting health risks; however these methods assume that health risks change dramatically at a given threshold value of birth weight. In reality, there is little evidence that such a threshold exists for excess fetal growth. Alternatively, approaching birth size as a continuum increases power to detect factors that influence birth size at the extremes, as well as within the normal range. For continuous analyses this dissertation uses birth weight z-scores (BWz), which are calculated as the observed minus the expected birth weight, divided by the standard deviation of birth weight from a population standard. The expected birth weight is derived from gestational age and

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gender specific growth curves, thereby controlling for these potentially confounding factors.[17]

EPIDEMIOLOGY OF LARGE INFANTS

The proportion of infants born macrosomic or LGA varies among populations from 5 to 20% and is highest in Nordic countries.[13, 18, 19] A sizable proportion of U.S. women give birth to large infants. Specifically, the incidence of LGA births (>90th percentile) ranges from ~6% among non-Hispanic Blacks, to 11% in non-Hispanic Whites, 8% in Hispanics, and 12% among Native Americans.[20]

Worldwide, there has been a 15-25% increase in the proportion of women giving birth to macrosomic/LGA infants over the past two decades.[18, 21-25] In the U.S., both mean birth weight and BWz increased in term-born white and black populations from 1985 to 1998.[26] The proportion of LGA births also increased from 11.5 to 12% for whites and from 6.5 to 7% among blacks (Hispanic ethnicity not considered).[26] These increases in birth weight and rates of LGA were only observed among term births. Pre-term and post-term births demonstrated small reductions in birth weight, BWz, and rates of LGA during this time-frame in the U.S.[26]

MATERNAL AND OFFSPRING HEALTH RISKS ASSOCIATED WITH HIGH BIRTH WEIGHT

Delivering a large infant is associated with several adverse health outcomes for both the mother and her offspring. Maternal risks associated with delivery include prolonged/assisted delivery, vaginal, cervical, and/or perineal lacerations, emergency cesarean delivery, and abnormal hemorrhage.[13, 16, 27-29] Vital records data indicate that risks for obstetric complications increase with progressively large infants.[30] For example,

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the odds of cesarean delivery increases about 1.5 times (OR=1.6, 95%CI= 1.61-1.63) when giving birth to an infant of 4.00-4.49 kg compared to a birth weight of 3.00-3.99 kg, while a birth weight of 4.50-4.99 kg is associated with more than twice the risk of cesarean (OR=2.6, 95%CI= 2.58-2.64) and a birth weight ≥ 5.00 kg has more than four times the risk (OR=4.7, 95%CI=4.54-4.83).[30] Long-term maternal health outcomes associated with giving birth to a macrosomic/LGA infant include anal dysfunction and general perineal defects.[13, 31] However, the permanence and/or clinical significance of childbirth-related pelvic floor trauma among the US population remain unclear.[32]

Macrosomic/LGA infants face an increased risk of birth trauma during delivery.[4, 13, 21, 30, 33] Vital data from 1995-1997 indicate that infants born at 4.00-4.50 kg have twice the risk of birth injuries as infants born 3.00-3.99 kg (OR=2.0, 95%CI=1.92-2.05), while those weighing 4.50-4.99 kg have more than three-times the risk (OR=3.1, 95%CI=2.96-3.32) and birth weight ≥ 5.00 kg is associated with 4.5-fold increased risk of trauma (95%CI=3.95-5.19).[30] The most common birth injuries include shoulder dystocia and resulting plexus injuries.[4, 34] Shoulder dystocia is estimated to complicate ~2% of all vaginal deliveries; however, when birth weight exceeds 4.5 kg this risk increases to 9-24% among non-diabetic women and 20-50% among diabetic pregnancies.[35] The risk of brachial plexus injury is approximately 18- to 21-fold higher among macrosomic infants compared to normal birth weight infants as well.[35]

Aside from injuries sustained at birth, macrosomic/LGA infants have an increased risk of congential anomalies, hypoglycemia, hyaline membrane disease, and meconium aspiration [13, 30, 36] Additionally, national data indicate that optimum birth weight occurs between 3.0-4.0 kg, above which mortality rates begin to increase.[37] Analyses of U.S.

infant death files support that infants with a birth weight ≥ 5.00 kg have a 2.7 increased odds of neonatal death (95%CI=1.91-3.80) compared to normal weight infants.[30]

Most injuries sustained during birth resolve as the infant matures; however, there is evidence that macrosomic/LGA infants have increased body fatness at birth when compared to normal weight infants.[5, 38, 39] This increased fatness appears to persist into childhood, placing macrosomic/LGA infants at greater risk for obesity and metabolic disease later in life.[1-3, 40-42] Other long-term outcomes associated with macrosomia/LGA have included high blood pressure/hypertension in adolescence and adulthood, as well as childhood cancer.[43-45] Thus, accumulating evidence suggests that size at birth, and in particular, body composition at birth, represent important determinants of later health outcomes.[46, 47]

FACTORS RELATED TO INFANT SIZE AT BIRTH

While several factors contribute towards explaining birth size, the true determinants are poorly understood. Non-modifiable factors related to birth size include parity, fetal sex, maternal age, maternal height, maternal race, and genetics.[13] Mean birth weight increases with successive births and it appears that parity is also associated with increased neonatal fat mass.[5, 48] In addition, male sex, maternal age, maternal height, and Caucasian race or Hispanic ethnicity are all associated with increased mean birth weight and/or LGA.[16, 49-53]

Aside from the factors discussed in the previous paragraph, genetic influences may account for 30-80% of the variation in birth size.[50, 54] In attempts to isolate genetic factors, researchers have shown that fetal insulin, insulin-like growth factor (IGF)-I, IGF-II, and associated receptors are critical for normal fetal growth.[50, 54, 55] Elevated levels of

fetal insulin and IGF-I have been associated with increased risk for macrosomia.[50] It is likely that complex interactions between parental, placental, and fetal genes exert influences on fetal growth.[13, 54, 55]

Several modifiable factors have also been associated with size at birth, including pregnancy complications, maternal anthropometrics, and lifestyle-related behaviors. Diabetes during pregnancy (pre-gestational or gestational) increases risk of macrosomia/LGA and is also associated with increased neonatal fat mass.[30, 56] Even when examined on a continuous scale, increased maternal serum glucose levels are associated with increased birth weight.[57] Overweight pre-pregnancy body mass index (BMI) and excessive weight gain are both related to increased birth weight and risk of LGA.[5, 6, 11, 51] In fact, population-based data indicate that once the increasing prevalence of maternal overweight and decreasing prevalence of maternal smoking are accounted for, temporal trends for increased incidence of LGA are no longer apparent, underscoring the importance of these two factors in the development of birth size.[22, 24]

Aside from smoking during pregnancy, other lifestyle factors such as maternal nutrition and LTPA appear to influence birth size. Investigations on the Dutch famine of 1944-1945 have shown that undernutrition during pregnancy does not affect birth weight unless total caloric intake drops below 1500 kilocalories in the third trimester.[58, 59] A recent study of 553 women in a developed country showed that total energy intake and/or percent macronutrient intake were not significantly related to risk of extreme birth weight.[11] However, the influence of maternal nutrition on birth weight variation within the normal range and subsequent adult health remains a subject of intense scientific debate.[60] Relationships between LTPA during pregnancy and birth size are complex and

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will be discussed in detail below. Overall, it appears that LTPA during pregnancy reduces fetal growth modestly, without increasing the risk of low birth weight.[7, 8] Other factors such as socioeconomic status/income and marital status have been hypothesized to affect birth size, but the evidence thus far is equivocal.[5, 49, 61, 62]

Despite a long list of variables associated with birth size, no single factor can accurately predict birth weight. The strongest modifiable risk factors for macrosomia/LGA across populations include pre-pregnant maternal overweight status, high pregnancy weight gain, and the presence of diabetes during pregnancy.[22, 63, 64] While women with decreased glucose tolerance deliver larger infants,[57, 65-68] diabetic pregnancies account for only a small percentage of LGA births due to the comparatively low incidence of gestational diabetes (~6%) and/or the prevalence of pre-pregnancy diabetes (~0.5%).[63, 69] In contrast, since ~52-60% of females of childbearing age are overweight,[70] maternal size accounts for substantially more LGA births.[63] Thus the influences of maternal size on birth size are presented in more detail below.

MATERNAL SIZE AND INFANT SIZE AT BIRTH

Epidemiology of Maternal Overweight Status and Gestational Weight Gain

Despite known health risks associated with overweight, the prevalence of overweight/obesity among U.S. adults has continued to increase in recent years.[71] Data from the Pregnancy Risk Assessment Monitoring System (PRAMS) from 26 states and New York City indicate that 23% of women are classified as overweight pre-pregnancy and 19% are obese according to BMI values calculated from self-reported data.[72] State-specific prevalences range from 20-25% overweight and 14-24% obese.[72]

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In 1990, the Institute of Medicine published guidelines for gestational weight gain according to pre-pregnancy BMI in an effort to optimize birth weight between 3.0-3.9 kg (Table 2.1).[73] Research supports that gaining weight within the recommended ranges is associated with lower risk of delivering a SGA or LGA infant.[74] Observational data also indicate that achieving a healthy weight gain within recommended amounts isassociated with decreased risk of preterm delivery, pregnancy complications such as pre-eclampsia, and adverse neonatal outcomes such as hypoglycemia and meconium aspiration.[74] Recent research indicates that pregnancy outcomes for obese women may be optimized with less than recommended or even no weight gain. Results from a population-based cohort study in Missouri found that risk for pre-eclampsia, cesarean delivery, SGA, and LGA were lowest when class I obese women (BMI 30-<35 kg/m^2) gained 10-25 lb, class II obese women (BMI 35-<40 kg/m^2) gained 0-10 lbs, and class III obese women (BMI 40+ kg/m^2) lost 2-10 lbs during pregnancy.[75]

Table 2.1: 1990 IOM Recommended Gestational Weight Gain Ranges According to Pre-Pregnancy Weight Status [73]

Pre-pregnancy BMI (kg/m^2)	**Weight Gain (lbs)**
Low (<19.8)	28-40
Normal (19.8-26.0)	25-35
Overweight (>26.0-29.0)	15-25
Obese (>29.0)	≥ 15

Unfortunately, U.S. data indicate that only ~30% of pregnant women gain weight within recommended ranges, while ~46% gain excess amounts and ~23% have less than recommended weight gain during pregnancy.[74] The prevalence of recommended weight gain is remarkably similar across populations, with studies involving Hispanic and/or multi-ethnic samples reporting similar rates.[76-78] Pre-pregnancy BMI influences

gestational weight gain with overweight women being two times more likely to gain excess weight as compared to normal weight women.[74, 78]

Relationships Among Maternal Anthropometric Variables and Infant Birth Size

Maternal height, weight, BMI prior to pregnancy, and gestational weight gain are each positively related to birth size, even with adjustment for sociodemographic factors and metabolic conditions.[5, 6, 49, 51, 63] Two smaller studies have also indicated that maternal overweight/obesity is associated with significantly greater neonatal fat mass and percent fat, even when overall birth weight is unaffected.[79, 80] Timing of gestational weight gain may also be important. Weight gain experienced from the first to second trimester is significantly related to infant length at birth, while weight gain from the second to third trimester is related to birth weight.[81, 82]

Because pre-pregnancy weight status and gestational weight gain are strongly correlated, it is difficult to determine their independent influences on birth weight. While pre-pregnancy weight status and gestational weight gain appear to have both independent and combined influences on fetal growth,[6] research supports that the overweight/ obese women who gain the most weight deliver the largest infants.[5, 49, 83] Maternal size and pregnancy weight gain may affect fetal growth by enhancing placental size and influencing placental capacity to supply nutrients to the fetus.[84, 85] Additionally, changes in lipid metabolism that accompany overweight status may also affect birth size. Clausen et al. found that high levels of leptin, a hormone involved in lipid metabolism, in maternal serum during the second trimester were associated with a birth weight greater than 4.5 kg; however, leptin concentrations were no longer significantly related after adjustment for maternal BMI.[86]

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The exact pathways through which maternal size and/or weight gain influences fetal growth are not yet understood; however, they are likely to be multi-factorial and involve interactions with genetic and environmental factors. Unfortunately, studies examining the contribution of maternal size and pregnancy weight gain on birth weight have rarely accounted for the influence of LTPA, which may affect both maternal and infant body size/composition. One recent study of 553 Scandinavian women found that while maternal BMI, weight gain, plasma glucose, gestational age and maternal LTPA were each independently related to risk of macrosomia, only low-level pre-pregnancy LTPA remained a significant predictor of macrosomia in adjusted analysis.[11] These results indicate that maternal LTPA is a modifiable determinant of birth weight and may interact with maternal anthropometric influences.

MATERNAL PHYSICAL ACTIVITY DURING PREGNANCY

The American College of Obstetricians and Gynecology (ACOG) published the first U.S. guidelines for exercise during pregnancy in 1985.[87] These original guidelines were cautious and advised women to keep their heart rate below 140 beats per minute and to limit "strenuous activity" to 15 minutes in duration.[87] Specific concerns about potential adverse effects of maternal exercise included abortion, growth restriction, premature labor, fetal hypoxia, acidosis, hyperthermia, and brain damage.[88] Since that time, literature has shown that LTPA generally does not increase risk of adverse pregnancy outcomes, and may be associated with a wide range of maternal and fetal health benefits.[88-90] Thus, the most current ACOG guidelines (2002) recommend that all pregnant women participate in at least 30 minutes of moderate LTPA on most days of the week.[91] These guidelines also state that recreational and competitive athletes may

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maintain their activities during pregnancy with medical supervision. Thus, vigorous intensity activity is not constrained and the pregnant woman is left to the discretion of her health care provider and herself to modify activity as needed. In fact, the only activities which ACOG recommends against are recreational sports with a high potential for contact or falls, scuba diving, and prolonged activity in the supine position, all of which are associated with risk for fetal trauma or impaired venous return.[91] Most recently the U.S. Government has released evidence-based LTPA guidelines for all Americans.[92] In accordance with the 2002 ACOG guidelines, these governmental guidelines state that women who are not already active should get at least 150 minutes of moderate aerobic activity per week during pregnancy, and women who habitually engage in vigorous activity may continue to do so provided they discuss their activities with their health care provider.

Epidemiology of Physical Activity during Pregnancy

About two-thirds of pregnant women in the U.S. choose to engage in some amount of LTPA, but only 16% participate at recommended levels.[93] Among active women, the most commonly reported LTPA during pregnancy is walking (~43-53%), followed by swimming (~12%) and aerobics (~10-12%).[93, 94] Few investigators have examined participation in vigorous LTPA. Using population-based data, ~6% of pregnant women report running in the past month while ~1% report playing team or racquet sports.[93] A study of almost 1700 women found that 14% reported vigorous activities in the first trimester, while only 8% participated in vigorous activity in the second trimester.[95]

Most population-based reports of LTPA participation during pregnancy do not account for gestational length; however, it is known that participation in exercise/LTPA decreases with increasing gestation.[96-99] A study conducted in the Boston, Massachusetts area (n=1442) using 7-day recall measurements of LTPA, showed that mean levels of LTPA decreased from 9.6 to 6.9 hours/wk during pregnancy.[100] Additionally, the prevalence of not meeting ACOG guidelines increased from 13% pre-pregnancy to 22% during the second trimester.[100] Another study of 250 women that measured several domains of physical activity found that median total energy expenditure remained fairly stable throughout pregnancy (~33 MET-hr/day), but that moderate activity energy expenditure was lower in the third trimester (0.8 MET-hr/day) compared to the first (2.3 MET-hr/day) while household/care giving energy expenditure was higher (6.8 vs. 12.5 MET-hr/day for the first vs. the third trimester, respectively).[98] Thus it is possible that pregnant women replace more strenuous physical activities with lighter activities as the pregnancy progresses.

Several maternal characteristics are associated with LTPA participation during pregnancy. Non-Hispanic white race/ethnicity, nulliparity, >high school education, older maternal age (>25 years), not smoking, and engaging in structured exercise pre-pregnancy are all associated with increased odds of participating in LTPA during pregnancy.[96-98, 101] Factors associated with decreasing LTPA participation during pregnancy include parity, young maternal age, overweight pre-pregnancy BMI, low self-efficacy for LTPA, and high frequency of pre-pregnancy LTPA.[97, 100, 102] Reported barriers to LTPA during pregnancy include fatigue, lack of time, nausea, physical discomfort, and lack of child care.[103-106] Studies also indicate that some women fear that

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exercise might hurt their baby and perceive vigorous/ high-impact activities as unsafe.[105, 107-109] While women appear to recognize the health benefits of participating in LTPA, most rate rest and relaxation as more important than exercise during pregnancy.[109]

Health Benefits of Physical Activity during Pregnancy

Several maternal and fetal health benefits associated with LTPA during pregnancy have been documented. Reviews of literature published over the past two decades suggest that participation in LTPA before and/or during pregnancy is associated with decreased risk for gestational diabetes, pre-eclampsia, and preterm delivery.[88-90, 110-113] Some debate exists surrounding the timing of LTPA needed for beneficial effects. For gestational diabetes, the strongest protective effect occurs with LTPA participation both before and during pregnancy.[113] Additionally, LTPA during pregnancy has been found to be a safe and efficacious treatment for controlling blood sugar within normal limits among women who are already diabetic or become so during pregnancy.[88, 114, 115] Similarly, participation in LTPA both before and during pregnancy yields the strongest protective effect against pre-eclampsia.[113] Although data are limited, it appears that participation in vigorous LTPA during pregnancy is also related to decreased risk for pre-term birth; however these results are based only on observational data.[95, 116]

While observational studies show clear benefits associated with maternal exercise, results from randomized trials are less conclusive. Cochrane reviews have found insufficient evidence for a protective effect of maternal exercise on the risk of either pre-eclampsia or gestational diabetes.[117, 118] It is important to note that very few studies have attempted to randomize exercise programs during pregnancy and that these have included

small samples (n=16 to 38 women per study). Thus, larger intervention studies with more power to detect results are needed before conclusions are made.

Proposed mechanisms for the effect of maternal exercise on the prevention of maternal disease include enhanced placental growth and vascularity, reduced oxidative stress, reduced inflammation, improved endothelial function, and improved blood lipids.[88, 90] It is also likely that differences in underlying maternal fitness, pre-pregnancy weight status, and gestational weight gain may partially account for lower rates of gestational diabetes and pre-eclampsia among women who are active during pregnancy versus those who are not. More research is needed to clarify etiological pathways for the health benefits of LTPA during pregnancy.

MATERNAL PHYSICAL ACTIVITY AND INFANT SIZE AT BIRTH

Evidence for the effects of LTPA during pregnancy on birth size is conflicting. While some studies show that LTPA during pregnancy decreases birth weight,[119, 120] others report increases in birth weight,[121] some find no effect,[122-124] and still others report a "U-shaped" association such that both high and low levels of LTPA decrease birth weight.[125] These apparently conflicting results are likely due to methodological differences in assessing LTPA, a lack of control for appropriate confounders, and variability in the choice of insufficiently active vs. completely sedentary control groups.[113, 126, 127] However, inconsistent results might also reflect real differences between populations of pregnant women. While controlling for several maternal demographic characteristics, past studies have failed to account for LTPA participation *prior* to pregnancy,[121, 122] have measured LTPA in only one or two trimesters,[122, 125, 128] or have been based on small and/or non-diverse samples.[120-122, 124, 125] Despite these obstacles, the

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majority of evidence suggests that LTPA during pregnancy decreases birth weight modestly within the normal range.[89, 126]

To date, few studies have specifically considered the effect of LTPA during pregnancy on macrosomia/LGA. One study among 291 Coloradan women found that participation in ≥ 2 hrs/wk of at least moderate LTPA in the second or third trimesters reduced risk of LGA (OR=0.3, 95%CI=0.2-0.7) with no effect SGA (OR=0.8, 95%CI=0.3-2.3).[8] A study on modifiable determinants of macrosomia (defined as ≥4.2 kg in this study) among 553 Norwegian women found that LTPA during pregnancy was unrelated to birth weight, but that low LTPA pre-pregnancy (<1 hr/wk) increased risk of macrosomia (aOR=2.9, 95%CI: 1.2-7.3).[11] An imprecise definition of LTPA participation which lacked information on intensity may have contributed to an inability to find more significant results for LTPA during pregnancy in this study.

A recent prospective cohort study among Danish women found no association between participation in sports/LTPA during the second or third trimesters of pregnancy and macrosomia (defined as ≥4.5 kg).[129] It appears that only ~3% of women in the Danish study gave birth to macrosomic infants, as compared to the higher prevalence of LGA/macrosomia reported in the Coloradan study (12%) and in the Norwegian study (15%).[8, 11, 129] Furthermore, the Danish study classified LTPA by categories of hours/week spent in sport or by categories of sport type (i.e. weight bearing vs. non-weight bearing). Thus, discrepancies in results may be due to underlying differences in the birth weight distributions and/or to methodological differences in defining LTPA during pregnancy.

In sum, preliminary evidence from the few studies to examine LTPA during pregnancy in relation to extreme high birth weight suggest either a null relationship or a protective effect that helps to modulate birth size within the normal range. Providing some additional support, Perkins et al.[7] found that total physical activity averaged over the second and third trimesters was strongly inversely correlated with fetal growth ratio, a measure of birth size adjusted for potential confounders ($r = -0.42$, $p<0.01$), particularly among taller women. While only 51 women were involved in the Perkins et al. study, total physical activity during pregnancy was objectively measured using accelerometry, thereby freeing their results from responder and/or recall bias.[7] These results await confirmation from a larger, more diverse study with greater ability to adjust for confounding variables.

Compared to LTPA, job-related physical activity during pregnancy appears to have lesser effects on birth size.[130] More time spent working and in shift work contribute towards small decreases in birth weight and borderline significant increased risk of giving birth to a SGA infant.[130-133] Job-related physical activity may result in different physiological responses than those that occur with rhythmic aerobic LTPA such as walking for exercise. Thus, it is not surprising that shift work and long periods of standing at work have been associated with detrimental pregnancy outcomes, while the majority of evidence for LTPA during pregnancy points towards beneficial effects.[88, 130-133] It is beyond the scope of this dissertation to fully review the literature regarding job-related physical activity and pregnancy outcomes; however, the amount of time spent working and basic job characteristics are important to assess as covariates when examining affects of pregnancy LTPA on birth size.

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Mechanism of Affect of Physical Activity on Birth Size

To enable fetal growth, the mother must supply precursors for placental hormone products as well as nutrients/substrates.[134] In a normal pregnancy, increased availability of metabolic substrate occurs mainly in the second and third trimesters, when fetal growth accelerates. As pregnancy advances, maternal insulin resistance and lipolysis are promoted while blood glucose levels are increased to ensure feto-placental growth.[134] In addition, women experience a blood volume expansion early in pregnancy to increase cardiac output and perfuse the placenta.[135] The placenta in turn transports nutrients to the growing fetus through simple or facilitated diffusion, the promotion of transplacental concentration gradients, and the production of alternate substrates delivered via the umbilical circulation.[134] Both pregnancy in and of itself, as well as maternal exercise, require increased blood flow, substrate delivery, and waste disposal. The response of a pregnant woman to exercise must therefore balance both maternal and fetal needs.

Physical activity during pregnancy is thought to affect fetal growth by reducing placental blood flow and nutrient delivery to the fetus *during exercise* as blood is diverted towards the working muscle.[136] Nonetheless, regular participation in LTPA throughout pregnancy results in an overall increase in blood volume thereby enhancing nutrient delivery to the fetus *at rest*.[135, 136] A woman with a history of regular LTPA may also start her pregnancy with above average blood volume, promoting fetal nutrient delivery. Thus, knowledge of pre-pregnancy LTPA habits is critical for interpreting the effects of LTPA during pregnancy on the developing fetus. To complicate matters further, the effect of LTPA on fetal growth may be trimester-specific. Maintaining an exercise program late in pregnancy appears to reduce fetal growth, while reducing exercise volume in late

gestation enhances fetal growth, especially fat mass.[120] A review article on the effects of exercise on feto-placental growth concluded that influences are time-specific and dependent on the frequency, duration, and intensity of exercise; however, it appears that regular moderate to vigorous exercise throughout pregnancy is associated with having a lighter, leaner infant.[136] The maintenance of exercise during pregnancy also improves insulin sensitivity at rest, thereby presenting the placenta with normal, rather than elevated, blood glucose levels.[88]

In conclusion, LTPA before and during pregnancy may decrease birth size moderately and reduce the risk of having a large infant without increasing the risk of delivering a small infant; however, these results await confirmation from larger and better designed studies.[7, 8, 137] In particular, previous studies of LTPA during pregnancy have utilized primarily homogeneous samples of healthy Caucasian women. Additionally, the majority of research on this topic is observational and the potential for self-selection biases cannot be ignored. Finally, much of the past literature has not measured LTPA with sufficient detail and precision to calculate energy expenditure and/or examine differing health effects associated with specific modes of activity.

MATERNAL SIZE, MATERNAL PHYSICAL ACTIVITY AND INFANT SIZE AT BIRTH

Recently a study of 223 Swedish women (response rate 19%) demonstrated that pre-pregnancy LTPA is significantly related to gestational weight gain.[138] Among this cohort, low pre-pregnancy LTPA was associated with excess gestational weight gain; however, LTPA was not associated with pre-pregnancy BMI or birth weight. Another study of 467 Norwegian women (85% response rate) found that a significantly lower

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proportion of women who exercised at least four times per week had a gestational weight gain of >16 kg (35.2 lbs) in the third trimester when compared to women who exercised less frequently.[139] Neither of these studies investigated potential interactive effects of maternal size, weight gain, and LTPA participation on birth size.

It is reasonable to expect interactive effects between maternal size and LTPA on birth size. Research indicates that mothers with high pre-pregnancy BMI and/or high gestational weight gain deliver excess amounts of nutrients and insulin to their developing fetus, leading to higher birth weight.[79] Mechanistically, LTPA would be expected to promote glucose utilization within the working muscle and enhance insulin sensitivity, thereby reducing the mother's tendency to "overfeed" her fetus. Thus, maternal size may influence offspring birth size to a lesser extent among active women when compared to low-active/sedentary women. In fact, a recent study has shown that, maternal BMI and weight gain are no longer significantly related to odds of delivering a macrosomic infant once pre-pregnancy LTPA is included in the model.[11] Possible interactive affects of LTPA with maternal size on birth weight on a continuous scale have yet to be investigated.

SUMMARY

Appropriate fetal growth is critical to ensuring healthy pregnancy and birth outcomes, yet predisposing factors related to giving birth to a large infant are poorly understood. The incidence of LGA births varies from 6 – 12% of U.S. pregnancies, depending on maternal race/ethnicity, and these infants are at increased risk of birth trauma and future overweight status.[1, 4, 37] Thus, determining modifiable risk factors for excess fetal growth leading to macrosomia/LGA has the potential to improve pregnancy

outcomes as well as elucidate possible intervention efforts for the prevention of childhood obesity.

The most consistently reported risk factors for macrosomia/LGA include gestational diabetes, maternal pre-pregnancy overweight status, and excess gestational weight gain.[22, 64] Leisure-time physical activity during pregnancy has also been shown to help control fetal overgrowth; however, these results are based on relatively small, select samples of women and await confirmation from larger, more diverse studies.[7, 8] The mechanism of effect for LTPA to control fetal overgrowth is unclear; however, there is some evidence that more active women have lower gestational weight gains.[138, 139] It also seems reasonable that LTPA would promote glucose utilization within the working muscle and enhance insulin sensitivity, thereby reducing the diabetic and/or overweight mother's tendency to "overfeed" her fetus. Recent results from 553 Norwegian pregnancies provide partial support for this hypothesis by demonstrating that maternal BMI is no longer related to odds of delivering a macrosomic infant once pre-pregnancy LTPA is also considered.[11] Inter-relationships among maternal size, gestational weight gain, LTPA participation during pregnancy, and birth size requires more attention. Preliminary results suggest that LTPA during pregnancy reduces overgrowth without shifting the entire birth weight distribution downward.[8] If these results are confirmed, future research may seek to examine the efficacy of LTPA intervention programs during pregnancy to reduce the risk of giving birth to a macrosomic/LGA infant without fear of increasing the risk for low birth weight/SGA.

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CHAPTER 3

MATERNAL PHYSICAL ACTIVITY DURING PREGNANCY AND THE BIRTH WEIGHT DISTRIBUTION: WHERE IS THE EFFECT?

ABSTRACT

This study sought to characterize the relation between leisure-time physical activity (LTPA) during pregnancy and birth weight. Women enrolled in the Pregnancy Outcomes and Community Health Study (1998-2004) were followed-up in 2007. Follow-up efforts were extensive for a subcohort and minimal for the remainder, or non-subcohort. As a result, 596 (67% of eligible) subcohort and 418 (26% of eligible) non-subcohort women who delivered at term were included in this investigation. Original data collection provided maternal demographics. Medical records provided child gender, gestational age, and birth weight. Gender and gestational age-specific birth weight z-scores (BWz) were calculated and offspring were categorized as small-, appropriate-, or large-for-gestational-age (SGA, AGA, and LGA, respectively). At follow-up, women recalled pregnancy LTPA and were classified as inactive, insufficiently active (< 7.5 kcal/kg/wk), and meeting LTPA recommendations (≥ 7.5 kcal/kg/wk). Analyses were conducted separately by subcohort status. The subcohort had greater racial and socioeconomic diversity than the non-subcohort. Among the non-subcohort, meeting LTPA recommendations significantly decreased odds of LGA (aOR=0.30, 95%CI: 0.14-0.64) without affecting odds of SGA. In quantile regression analyses, meeting LTPA recommendations was unrelated to BWz until the 0.65 quantile, after which it significantly reduced BWz. Results for the subcohort were similar but non-significant.

LPTA during pregnancy may represent a significant health benefit by reducing BWz only among the upper parts of the distribution.

INTRODUCTION

The American College of Obstetricians and Gynecologists (ACOG) recommends that all pregnant women participate in at least 30 minutes of moderate leisure-time physical activity (LTPA) on most days of the week in the absence of obstetrical complications.[1] Recent governmental LTPA recommendations also endorse at least 150 min/wk of at least moderate LTPA for pregnant women.[2] Population-based data indicate that the majority of pregnant women (~66%) choose to engage in some amount of LTPA, but only 16% participate at recommended levels.[3]

While LTPA during pregnancy has been associated with several maternal health benefits including decreased risk for gestational diabetes, pre-eclampsia, and preterm delivery, effects on birth weight are still debated.[4-9] Research has shown repeatedly that LTPA during pregnancy does not increase risk of delivering a low birth weight infant.[5, 7, 10] However, results with mean birth weight have been more varied, with some reporting no changes, others finding significant reductions in mean birth weight, and one study showing increased mean birth weight associated with vigorous exercise during pregnancy.[7, 11-13]

Very few studies have considered the effect of LTPA during pregnancy on high birth weight. One small study found that participation in LTPA later in pregnancy (2^{nd} or 3^{rd} trimester) significantly reduced odds of giving birth to a large-for-gestational-age (LGA, $\geq 90^{th}$ percentile) infant without affecting risk of delivering small-for-gestational-age (SGA, $<10^{th}$ percentile).[14] However, results from a recent cohort study showed no associations among sports/LTPA participation and odds of giving birth to a high birth weight infant (≥ 4.5 kg).[15] Giving birth to a large infant is associated with several adverse

health outcomes including prolonged and complicated deliveries for the mother, as well as increased risk of birth trauma and future childhood obesity for the offspring.[16, 17] Thus, if LTPA during pregnancy could decrease the risk of giving birth to a large infant without shifting the entire birth weight distribution downwards, this could represent a significant health benefit.

The purpose of this study was to more fully characterize the effect of LTPA during pregnancy on offspring size at birth among a diverse group of women who delivered at term (≥ 37 weeks). Specifically, we sought to determine whether LTPA during pregnancy was associated with a mean shift in the entire birth weight distribution, whether it was associated with giving birth to an SGA or LGA infant, and whether there was an isolated effect of LTPA during pregnancy on the high end of the birth weight distribution.

METHODS

Study Population

This study followed-up women enrolled in the Pregnancy Outcomes and Community Health (POUCH) Study. Women were originally recruited in gestational weeks 15-27 from 1998-2004 from 52 clinics in five Michigan communities. Inclusion criteria were singleton pregnancy with no known congenital anomaly, maternal age ≥15 years, maternal serum alpha-fetoprotein screen in gestational weeks 15-22, no pre-existing diagnoses of diabetes mellitus, and proficiency in English. Women with unexplained high alpha-fetoprotein levels (≥ 2 multiples of the median) were oversampled due to a particular interest in this biomarker for the original POUCH study aims.[18] Of the 3,038 women enrolled, 19 were lost to follow-up at birth leaving a cohort

of 3,019 mother-child pairs. The POUCH study was approved from institutional review boards at Michigan State University, Michigan Department of Community Health, and nine community hospitals.

A subcohort of women was selected for more detailed study to maximize resources when evaluating original study aims. The subcohort included all women who delivered preterm (<37 weeks), women who delivered at term but had unexplained high maternal serum alpha-fetoprotein levels, and a race-stratified sample of women with term deliveries and normal maternal serum alpha-fetoprotein levels (i.e., 72% African American and 23% White/other women in this category). Women enrolled in POUCH but not meeting these criteria comprised the "non-subcohort". Women in the subcohort were contacted periodically for different follow-up studies (2005-2006; 2006-2007), while the non-subcohort received minimal contact.

In fall of 2007, follow-up surveys on LTPA during pregnancy and child health outcomes were sent to all POUCH participants who had not declined further contact after delivery and whose children were living with them (n=1629 non-subcohort; n=1261 subcohort). Women in the non-subcohort were sent a single mailing which asked them to complete and return an enclosed survey. No further contact was attempted for the non-subcohort. Women in the subcohort were sent the same mailing; however, phone contact was attempted to encourage participation and follow-up mailings were sent.

For this investigation, women who delivered preterm (< 37 weeks of gestation) were excluded (non-subcohort n=0, subcohort n=335). A total of 1200 non-subcohort and 299 subcohort women failed to return the follow-up survey, and there was incomplete follow-up information on LTPA during pregnancy (non-subcohort n=11, subcohort n=31)

Thus, the final sample for this investigation included 418 (26% of eligible) non-subcohort and 596 (67% of eligible) subcohort women.

Study Protocol

The POUCH study has been described elsewhere in detail.[18] Briefly, participants met with a study nurse at enrollment to sign consent forms, complete an in-person interview and a self-administered survey, and have biological samples collected. The interview and self-administered survey provided information on maternal size, race/ethnicity, education, relationship status, enrollment in Medicaid, occupational level (Low=Clerical/Sales, Service/Blue Collar, or Homemaker/Other/Unknown; High = Professional/Manager/Technical), and smoking at mid-pregnancy. Maternal pre-pregnancy body mass index (BMI, kg/m^2) was calculated from self-reported pre-pregnancy weight and height values.

Birth weight, child gender, maternal age at delivery, and parity were determined through chart review. Gestational age was calculated using the last menstrual period unless it disagreed by > 2 weeks with ultrasound conducted prior to 25 weeks gestation, in which case the ultrasound value was used. Sex and gestational-age specific birth weight z-scores were calculated as the observed minus the mean birth weight divided by the population standard deviation using birth weight standards from Kramer et al.[19] Offspring were classified as SGA, appropriate-for-gestational-age (AGA), or LGA if their sex and gestational age-specific birth weight was $\leq 10^{th}$, between the 10^{th} and 90^{th}, or $\geq 90^{th}$ percentile, respectively.[20]

The follow-up survey provided information on gestational weight gain and LTPA (Appendix). Time from delivery to follow-up was used to determine length of recall (<4,

4-<6, 6-9 years). Self-reported maternal weight gain during the POUCH pregnancy was used to classify women into weight gain categories (less than, within, and greater than recommended) based on the 1990 Institute of Medicine recommendations according to their pre-pregnancy BMI.[21]

Finally, women were asked whether they had participated in any LTPA during the POUCH pregnancy. If so, they recalled the type, average duration (min/d), and average frequency (d/wk) of up to two activities performed most often during a typical week while pregnant. To quantify intensity, metabolic equivalent (MET) values were assigned to each reported activity using the Compendium for Physical Activities.[22] MET values were converted to caloric energy expenditure (1 MET = 1 kcal/kg/hr), multiplied by reported duration and frequency values, and then summed within each woman to calculate total LTPA energy expenditure (kcal/kg/wk). Using this method, meeting ACOG recommendations for LTPA during pregnancy corresponds to expending ≥7.5 kcal/kg/wk, or 3 METs (i.e., the lower-bound of "moderate" intensity), times 30 min/day, times 5 days/wk, divided by 60 min/hr.[1, 22] For analyses, women were classified as inactive (0 kcal/kg/wk), insufficiently active (< 7.5 kcal/kg/wk), or meeting/exceeding LTPA recommendations (≥ 7.5 kcal/kg/wk) during pregnancy.

Statistical Analyses

Because of the sampling scheme employed to create the original POUCH study cohort and subcohort, and the differing follow-up strategies, analyses were conducted separately for non-subcohort and subcohort participants. All analyses were conducted using SAS version 9.1. Significance was set at a two-sided alpha level of $P \leq 0.05$. Linear, polytomous logistic, and quantile regression analyses were used to assess the

relation between LTPA during pregnancy (reference group = inactive) and birth size (modeled as birth weight z-score or size for gestational age categories). Stepwise regression methods were used to build adjusted models. The following variables were considered as covariates based on previous literature: maternal race (among the subcohort only), pre-pregnancy BMI, maternal height, gestational weight gain categories, parity, maternal report of smoking during pregnancy, enrollment in Medicaid, relationship status, maternal age at delivery, educational level, and occupational level. Any variable that altered parameter estimates more than 10% was examined as a potential confounder or mediator. All multivariate models included length of recall for LTPA during pregnancy.

Linear regression analyses (PROC GLM) were conducted first to determine whether LTPA during pregnancy was associated with a mean shift in the birth weight z-score distribution. Adjusted R^2 values were used to assess the amount of variance explained. Next, polytomous logistic regression (PROC LOGISTIC) was used to estimate associations among LTPA during pregnancy and giving birth to an SGA or LGA infant (reference category= AGA). Likelihood ratio tests were used for significance testing in building adjusted models.

Finally, quantile regression (PROC QUANTREG) was used to estimate the association between LTPA during pregnancy and the entire distribution of birth weight z-score. As an extension of median regression, quantile regression uses all available data to examine the effect of an independent variable on specified quantiles of the distribution of the dependent variable, not just the mean value.[23] Therefore, quantile regression can determine whether LTPA during pregnancy has a constant affect across the entire birth

weight z-score distribution, or has a variable affect on only certain parts. Unlike logistic regression, quantile regression does not require the transformation of birth weight into somewhat arbitrary categories of SGA, AGA, and LGA. Thus, quantile regression may provide insights into the effect of LTPA during pregnancy on birth size that are not revealed by linear or logistic regression techniques. We assessed the association between LTPA during pregnancy and birth weight z-score for every 0.05 quantile from the 0.05 to 0.95 quantile of the distribution. Histograms of the standardized residuals were evaluated to determine goodness of fit.

RESULTS

Within both the non-subcohort and subcohort, follow-up survey nonresponders includedsignificantly more women who were African American, younger age, had less than high school education, single, enrolled in Medicaid and smoked during pregnancy, compared to participating women (data not shown). Non-responders within the subcohort also had a higher percentage of SGA and a lower percentage of LGA births compared to participants.

Among participants, maternal characteristics differed between non-subcohort and subcohort women (Table 3.1). Some differences were expected by design (e.g. 4% non-subcohort vs. 34% subcohort women African American) and other differences may reflect self-selection. The subcohort included more women who were younger, less educated, single, enrolled in Medicaid, had higher pre-pregnancy BMI values, gained less weight than recommended, smoked during pregnancy, and worked in a " low" level occupation.

Mean birth weight was 3.51 ± 0.45 kg among the non-subcohort and 3.38 ± 0.49 kg among the subcohort, corresponding to mean z-scores of 0.24 ± 0.97 and -0.09 ± 1.04, respectively. While a similar proportion of infants were born AGA in both groups (~78%), 18% of non-subcohort infants were born LGA compared to 11% of subcohort infants. A similar proportion of women in each group were classified as meeting LTPA recommendations (31% v. 29% for non-subcohort v. subcohort); however, a lower percentage of non-subcohort women were classified as inactive (39%) as compared to subcohort women (48%). Average length of recall for LTPA during pregnancy was 5.2 ± 1.3 years for the non-subcohort and 5.4 ± 1.4 years for the subcohort.

Using unadjusted linear regression, we found that meeting LTPA recommendations was associated with a mean reduction in birth weight z-score among non-subcohort women (β= -0.23, $p<0.05$, Table 3.2). However, this relationship was no longer significant once adjusted for maternal height and pre-pregnancy BMI. The final model for the non-subcohort explained 16% of the variance in birth weight z-score and included LTPA during pregnancy, maternal height, pre-pregnancy BMI, gestational weight gain, parity, maternal age at delivery, and smoking during pregnancy. Within the subcohort, LTPA during pregnancy was unrelated to mean birth weight z-score. Other maternal characteristics, similar to those retained in the non-subcohort model, explained 18% of the variance in birth weight z-score in the full model (Table 3.2).

We next examined whether LTPA during pregnancy might be more related to extremes in birth weight. Being insufficiently active was not related to giving birth to either an SGA or LGA infant among both the non-subcohort and the subcohort (Table 3.3). Furthermore, meeting LTPA recommendations was not related to having an SGA

infant in either group. However, among the non-subcohort, meeting LTPA recommendations significantly reduced the odds (by 70%) of giving birth to an LGA infant even when adjusted for adequacy of gestational weight gain, maternal height, parity, occupational level, and recall length (aOR=0.30, 95%CI: 0.14-0.64). Among the subcohort, meeting LTPA recommendations also tended to be associated with lower odds of giving birth to an LGA infant; however, these associations were not statistically significant (OR=0.73, 95% CI: 0.39-1.36; aOR=0.78, 95%CI: 0.41-1.50).

We investigated the effect of LTPA during pregnancy on the birth weight z-score distribution using quantile regression and created quantplots to display the results (Figures 3.1-3.4). In quantplots, black circles represent parameter estimates for the effect of LTPA during pregnancy at every 0.05 quantile of the birth weight z-score distribution from 0.05 to 0.95. The gray shaded region represents the 95% confidence interval. Parameter estimates located below the zero line indicate a reduction in birth weight z-score and are considered to be significant for any region of the distribution in which the shaded 95% confidence interval does not include the zero line. A mostly flat line would indicate that LTPA during pregnancy has a constant effect on the entire distribution of birth weight z-score and would result in a mean shift of the distribution. In contrast, a curvilinear line would indicate that LTPA during pregnancy has isolated effects on specific portions of the distribution and may not result in a mean shift.

Figures 3.1 and 3.2 represent the association between LTPA during pregnancy and birth weight z-score among the non-subcohort. When considering insufficient LTPA during pregnancy, the shaded area of the quantplot includes the zero line across every quantile in both unadjusted (Figure 3.1a) and adjusted (Figure 3.2a) models, indicating a

null effect. Meeting LTPA recommendations also demonstrates a null relationship with birth weight z-score until the upper quantiles where the parameter estimates drop abruptly, indicating a reduction in birth weight z-score (Figure 3.1b). The adjusted model (Figure 3.2b) shows that meeting LTPA recommendations during pregnancy is essentially unrelated to birth weight z-score until the 0.65 quantile, after which it reduces birth weight z-score by up to 0.5 units.

Figures 3.3 and 3.4 represent quantile regression results among the subcohort. Results are similar to those observed for the non-subcohort but are not as statistically significant. While being insufficiently active appears to increase birth weight z-score among the mid range of the distribution in unadjusted analyses (Figure 3.3a), these results are no longer significant in the adjusted model (Figure 3.4a). Meeting LTPA recommendations during pregnancy shows the same pattern as the non-subcohort results in that parameter estimates indicate reduced birth weight z-scores among the upper quantiles (>0.65); however, the estimated effect is non-significant in both unadjusted (Figure 3.3b) and adjusted (Figure 3.4b) models. All analyses were re-run after removing women with high maternal serum alpha-fetoprotein levels and no substantial differences were seen (data not shown).

DISCUSSION

Our results indicate that meeting LTPA recommendations during pregnancy was not associated with a shift in the entire birth weight z-score distribution. Rather, LTPA at/above recommended levels decreased the odds of LGA and significantly decreased birth weight z-score above the 0.65 quantile among the non-subcohort. The subcohort demonstrated similar trends; however, their results were not statistically significant.

The descriptive characteristics of women in the non-subcohort and subcohort varied widely, with the subcohort generally displaying more racial/ethnic and socioeconomic diversity (Table 3.1). This is likely due to the race-stratified sampling scheme used to create the subcohort, as well as the extra efforts used to follow-up this group. Unmeasured confounding due to lifestyle factors that are not easily measured may be greater in diverse samples and could partly explain the attenuated effects of LTPA during pregnancy on birth size in the subcohort vs. non-subcohort. The subcohort had a lower percentage of LGA births (11%) compared to the non-subcohort (18%), thus differences in the statistical significance of our results may also reflect lower power within the subcohort to detect relationships between LTPA and odds of LGA.

While most (67%) of the subcohort participated in follow-up, only 26% of the non-subcohort returned the follow-up survey, and they did so in response to a single mailing. The non-subcohort therefore represents a more select group of women and their results may be less generalizable to other populations. However, previous literature has demonstrated that while non-responders may significantly differ from responders in regard to prevalence of exposure and outcome variables, the exposure-outcome associations are often similar in both groups if the study hypotheses are not suspected.[24, 25] While we were unable to assess the prevalence of LTPA participation among non-responders, the prevalence of LGA was lower among non-responders in both the non-subcohort (13% vs. 18% for non-responders vs. responders, $p=0.06$) and the subcohort (8% vs. 11% for non-responders vs. responders, $p<0.001$). Non-responders also tended to display greater racial/ethnic and socioeconomic diversity compared to responders in both groups. Despite selective follow-up, both the subcohort and non-subcohort showed the

same trend- meeting LTPA recommendations during pregnancy decreased odds of LGA and reduced birth weight birth weight z-score above the 0.65 quantile, without affecting mean birth weight. However, the effects were more robust and statistically significant only among the non-subcohort.

Our results support those previously found by Alderman et. al. who also examined LTPA during pregnancy in relation to risk of SGA or LGA. Studying a group of 291 Coloradan women, they found that participation in ≥2 hr/wk of at least moderate LTPA during pregnancy (i.e. the equivalent of ≥ 6.0 kcal/kg/wk) reduced risk of delivering an LGA infant (OR=0.3, 95%CI=0.2-0.7) with no effect on delivering an SGA infant (OR=0.8, 95%CI=0.3-2.3).[14] A study on modifiable determinants of high birth weight (≥4.2 kg) among 553 Norwegian women found that LTPA during pregnancy was unrelated to birth weight, but that low LTPA pre-pregnancy (<1 hr/wk) increased risk of high birth weight (aOR=2.9, 95%CI: 1.2-7.3).[26]

In contrast to our results, a recent prospective cohort study among Danish women found no association between participation in sports/LTPA during the second or third trimesters of pregnancy and high birth weight (≥4.5 kg).[15] It appears that only ~3% of women in the Danish study gave birth to high birth weight infants, as compared to the higher prevalence of LGA reported here (18% among the non-subcohort and 11% within the subcohort), in the Coloradan study (12%), and of high birth weight in the Norwegian study (15%).[14, 15, 26] Furthermore, the Danish study classified LTPA by categories of hours/week spent in sport or by categories of sport type (i.e., weight bearing vs. non-weight bearing). Thus, discrepancies in results may be due to underlying differences in

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the birth weight distributions and/or to methodological differences in defining LTPA during pregnancy.

Physical activity during pregnancy is thought to regulate fetal growth by helping normalize maternal blood glucose and by altering placental blood flow and nutrient delivery.[9, 27] Specifically, LTPA is associated with decreased placental blood flow intermittently during the exercise bout, but increased blood flow at rest due to training adaptations.[27, 28] While LTPA during the first and second trimesters appears to improve placentation and vascularization, LTPA during the third trimester may have the most direct effect on fetal growth.[27]

While we lacked trimester-specific information on LTPA during pregnancy, the use of quantile regression analyses in this study allowed us to refine existing knowledge of the association between LTPA during pregnancy and birth size. Our results showed a dramatic reduction in birth weight z-score associated with meeting LTPA recommendations during pregnancy, but only among the upper quantiles (>0.65). Higher birth weight is associated with short- and long-term health risks including birth trauma for both the mother and infant and increased risk for obesity and components of the metabolic syndrome during childhood.[16, 17, 29] Thus, our results suggest that LTPA during pregnancy may improve maternal/child health outcomes by helping to limit excessive fetal growth without reducing normal fetal growth.

Some limitations must be noted. Information on LTPA during pregnancy was recalled retrospectively by our participants 3-9 years postpartum, thus recall bias cannot be discounted. A previous study found strong correlations (r=0.57-0.85) among recalled and originally measured LTPA during pregnancy at six years postpartum.[30] However,

they had a select sample of mainly active women, thus their results may have limited generalizability. Bias due to recall error in our study may have been reduced by using a categorical LTPA variable with broadly defined groups. In addition, differential bias is less likely because women were not told of the study aims when they were asked to recall LTPA. We only queried women about LTPA performed during a "typical week" in pregnancy, thus we were not able to examine trimester-specific effects of LTPA on birth size. There is also still potential for unmeasured confounding because LTPA is correlated with other lifestyle factors, such as diet, that were not measured in this study.

Despite these limitations, our study adds significantly to the existing literature. This is the first time a quantile regression technique has been applied to an investigation of LTPA during pregnancy on birth weight, which allowed us to more precisely define the relationship. In addition, the unique follow-up strategy employed in the POUCH study allowed us to evaluate the LTPA- birth size relation in two different populations. Within the non-subcohort we were able to examine the effect of LTPA during pregnancy on birth size among a more homogeneous sample of women with potentially fewer confounding variables. In contrast, the subcohort allowed us to examine the relation in a diverse sample of women that is more generalizable to the U.S. pregnant population.

In conclusion, our results indicate that participating in LTPA during pregnancy at or above recommended levels is associated with lower risk for delivering an LGA infant, and reduces birth weight z-score among the higher quantiles of the distribution without causing a mean shift in the distribution. Due to the adverse maternal and child health effects associated with higher birth weight, our results may indicate a substantial health benefit for LTPA during pregnancy. Future studies with prospectively ascertained,

detailed measures of LTPA during each trimester of pregnancy are needed to test and refine our findings.

Table 3.1: Participant characteristics of the POUCH study non-subcohort and subcohort*

	Non-Subcohort N (%)	Subcohort N (%)	Chi-Square p-value
N	418	596	
Maternal Race			
White/Other	401 (96.0)	394 (66.1)	<0.001
African American	17 (4.1)	202 (33.9)	
Pre-pregnancy Maternal BMI			
< 25 kg/m^2	232 (55.5)	289 (48.5)	
25-<30 kg/m^2	112 (26.8)	139 (23.3)	<0.001
≥ 30 kg/m^2	74 (17.7)	168 (28.2)	
Maternal Height			
< 65 in	195 (46.7)	288 (48.3)	0.600
Gestational Weight Gain[$]			
Low	48 (11.5)	104 (17.5)	
Recommended	149 (35.7)	187 (31.4)	0.026
High	221 (52.9)	305 (51.2)	
Maternal Age at Delivery			
<20 yrs	23 (5.5)	60 (10.1)	
20-<30 yrs	202 (48.3)	346 (58.1)	<0.001
≥ 30 yrs	193 (46.2)	190 (31.9)	
Maternal Education			
< High School	34 (8.1)	89 (14.9)	
High School	77 (18.4)	154 (25.8)	<0.001
> High School	307 (73.4)	353 (59.2)	
Medicaid			
Yes	98 (23.4)	277 (46.5)	<0.001
Relationship Status			
Single	54 (12.9)	173 (29.0)	<0.001
Occupational Status[#]			
Low	281 (67.2)	457 (76.7)	<0.001
Smoking during Pregnancy			
At least some	33 (7.9)	92 (15.4)	<0.001
Parity			
Nulliparous	186 (44.5)	245 (41.1)	0.282
Child Gender			
Male	200 (47.9)	297 (49.8)	0.534

Table 3.1: (cont.)

	Non-Subcohort N (%)	Subcohort N (%)	Chi-Square p-value
Size at birth			
AGA	324 (77.5)	463 (77.7)	
SGA ($\leq 10^{th}$ %tile)	19 (4.6)	65 (10.9)	<0.001
LGA ($\geq 90^{th}$ %tile)	75 (17.9)	68 (11.4)	
LTPA During Pregnancy[†]			
Inactive	162 (38.8)	288 (48.3)	
Insufficiently Active	125 (29.9)	134 (22.5)	<0.005
Meeting LTPA Recs	131 (31.3)	174 (29.2)	

[*] Includes only POUCH study participants who gave birth at term and were enrolled in the 2007 follow-up study

[$] Based on IOM guidelines according to pre-pregnancy BMI

[#] Low Occupational Status = Clerical/Sales, Service/Blue Collar, or Homemaker/Other/Unknown

[†] LTPA= leisure time physical activity; "Inactive"=no LTPA during pregnancy, "Insufficiently Active"= LTPA during pregnancy less than the recommended (<7.5 kcal/kg/wk), "Meeting LTPA Recs"= LTPA during pregnancy at or above the recommended level (≥7.5 kcal/kg/wk)

Table 3.2: Linear regression analyses for the unadjusted and adjusted association between maternal LTPA during pregnancy and birth weight z-score by subcohort status.

	Non-Subcohort N=418	Subcohort N=596
Model 1: Adjusted R^2	**0.0103**	**0.0063**
LTPA[†]		
Insufficiently Active	-0.147 (-0.374, 0.080)	0.200 (-0.014, 0.431)
Meeting LTPA Recs	-0.232 (-0.457, -0.008)*	0.008 (-0.188, 0.204)
Model 2[‡]: Adjusted R^2	**0.0741**	**0.0510**
LTPA[†]		
Insufficiently Active	-0.085 (-0.310, 0.140)	0.180 (-0.031, 0.391)
Meeting LTPA Recs	-0.177 (-0.397, 0.043)	0.006 (-0.188, 0.200)
Maternal Height (in)	0.064 (0.032, 0.097)*	0.078 (0.047, 0.107)*
Pre-Pregnancy BMI (kg/m^2)	0.029 (0.014, 0.045)*	0.010 (-0.001, 0.021)
Model 3[‡]: Adjusted R^2	**0.1648**	**0.1840**
LTPA[†]		
Insufficiently Active	-0.077 (-0.297, 0.144)	0.071 (-0.128, 0.269)
Meeting LTPA Recs	-0.105 (-0.321, 0.110)	-0.010 (-0.193, 0.173)
Maternal Height (in)	0.050 (0.018, 0.082)*	0.064 (0.036, 0.092)*
Pre-Pregnancy BMI (kg/m^2)	0.034 (0.018, 0.049)*	0.017 (0.006, 0.028)*
Gestational Weight Gain (lbs)	0.015 (0.010, 0.021)*	0.008 (0.004, 0.013)*
Black Race (ref: White)	---	-0.325 (-0.497, -0.153)*
Nulliparous (ref: Parous)	-0.269 (-0.456, -0.082)*	-0.396 (-0.556, -0.237)*
Education (ref: < High School)	---	
= High School		-0.025 (-0.287, 0.237)
> High School		0.294 (0.051, 0.537)*
Age at Delivery (Ref: <20y)		---
20-<30 y	0.425 (0.015, 0.836)*	
≥ 30 y	0.492 (0.068, 0.917)*	
Smoking in Pregnancy	-0.360 (-0.690, -0.030)*	-0.481 (-0.704, -0.257)*

*significant p-value < 0.05

[†] LTPA=leisure-time physical activity (Ref: no LTPA during pregnancy), "Insufficiently Active"= LTPA during pregnancy less than the recommended (<7.5 kcal/kg/wk), "Meeting LTPA Recs"= LTPA during pregnancy at or above the recommended level (≥7.5 kcal/kg/wk)

[‡] Models 2 and 3 also adjusted for length of recall (<4, 4-<6, ≥6 yrs)

Table 3.3: Associations among maternal LTPA during pregnancy and appropriateness of size-for-gestational-age at birth (reference: AGA) by subcohort status.

	Non-Subcohort (n=418)			Subcohort (n=596)		
	Inactive[†]	Insufficiently Active[†]	Meeting LTPA Recs[†]	Inactive[†]	Insufficiently Active[†]	Meeting LTPA Recs[†]
SGA						
OR (95% CI)	1.0	1.92 (0.70-5.23)	0.29 (0.06-1.40)	1.0	0.67 (0.33-1.37)	0.93 (0.52-1.69)
aOR[$] (95%CI)	1.0	1.75 (0.59-5.16)	0.19 (0.04-1.05)	1.0	0.84 (0.40-1.80)	1.06 (0.57-1.99)
LGA						
OR (95% CI)	1.0	0.98 (0.56-1.73)	0.30* (0.15-0.61)	1.0	1.00 (0.54-1.87)	0.73 (0.39-1.36)
aOR[#] (95%CI)	1.0	1.03 (0.59-1.90)	0.30* (0.14-0.64)	1.0	0.88 (0.46-1.70)	0.78 (0.41-1.50)

*p<0.05

[†] LTPA=leisure time physical activity; "Inactive"=no LTPA during pregnancy, "Insufficiently Active"= LTPA during pregnancy less than the recommended (<7.5 kcal/kg/wk), "Meeting LTPA Recs"= LTPA during pregnancy at or above the recommended level (≥7.5 kcal/kg/wk)

[$] Non-Subcohort aOR's are adjusted for maternal weight gain during pregnancy (below, meeting, or over IOM recommendation based on pre-pregnancy BMI), maternal height (</≥ 65 in), parity (nulliparous/parous), maternal occupational level (Low/High), and years of recall (< 4, 4-<6, ≥ 6 yrs)

[#] Subcohort aOR's are adjusted for maternal race (black vs white/other), weight gain during pregnancy (below, meeting, or over IOM recommendation based on pre-pregnancy BMI), maternal height (</≥ 65 in), parity (nulliparous/parous), maternal education (less than, equal to, or more than high school), maternal smoking during pregnancy (yes/no), and years of recall (< 4, 4-<6, ≥ 6 yrs)

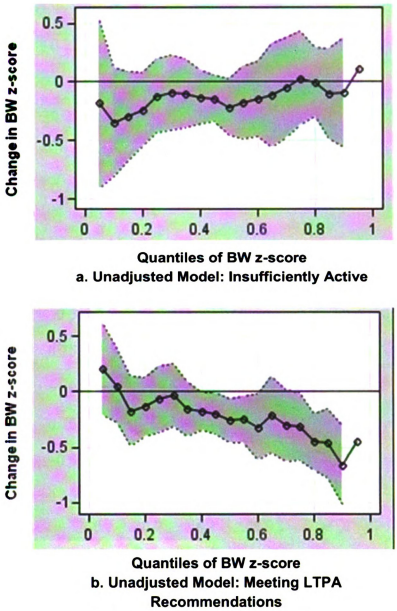
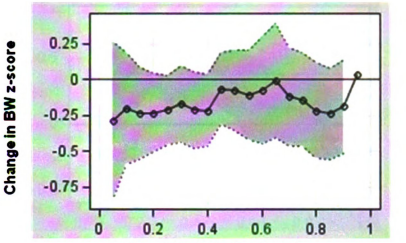
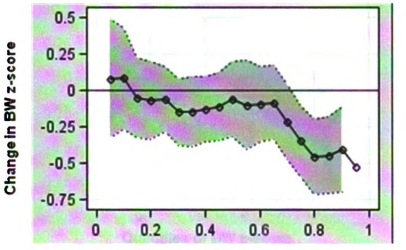


Figure 3.1: Unadjusted associations of LTPA during pregnancy and birth weight z-score among the POUCH study non-subcohort participants across quantiles. The black circles represent participant estimates while the gray shaded area represents the 95% confidence interval. Plots a and b show the unadjusted effect of being insufficiently active and meeting/exceeding LTPA recommendations on birth weight z-score, respectively.

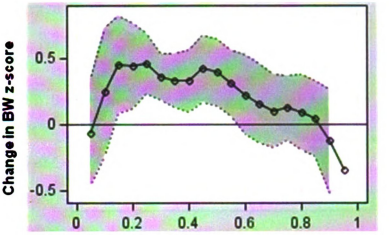


a. Adjusted Model: Insufficiently Active



b. Adjusted Model: Meeting LTPA Recommendations

Figure 3.2: Adjusted associations of LTPA during pregnancy and birth weight z-score among the POUCH study non-subcohort participants across quantiles. The black circles represent participant estimates while the gray shaded area represents the 95% confidence interval. Plots a and b show the effects of being insufficiently active and meeting/exceeding LTPA recommendations on birth weight z-score once adjusted for maternal weight gain during pregnancy (below, meeting, or over IOM recommendation based on pre-pregnancy BMI), maternal height (</≥ 65 in), parity (nulliparous/parous), maternal occupational level (Low/High), maternal age at delivery (<20, 20-<30, ≥ 30 yrs), smoking during pregnancy (yes/no), and years of recall (< 4, 4-<6, ≥ 6 yrs).



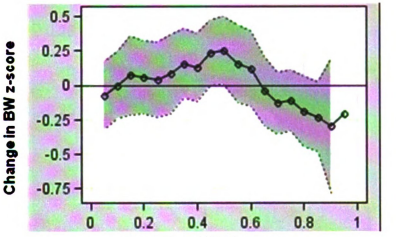


Figure 3.3: Unadjusted associations of LTPA during pregnancy and birth weight z-score among the POUCH study subcohort participants across quantiles. The black circles represent participant estimates while the gray shaded area represents the 95% confidence interval. Plots a and b show the unadjusted effect of being insufficiently active and meeting/ exceeding LTPA recommendations on birth weight z-score, respectively.

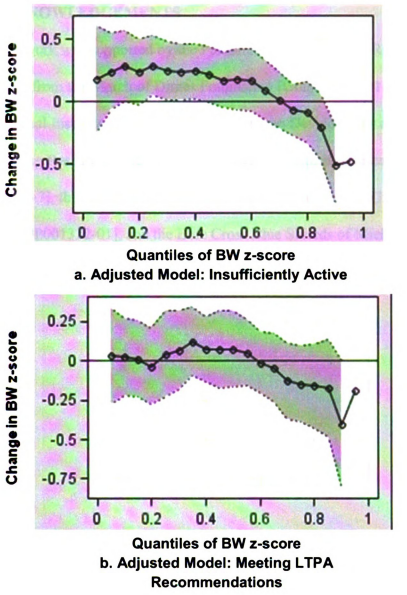


Figure 3.4: Adjusted associations of LTPA during pregnancy and birth weight z-score among the POUCH study subcohort participants across quantiles. The black circles represent participant estimates while the gray shaded area represents the 95% confidence interval. Plots a and b show the effects of being insufficiently active and meeting/ exceeding LTPA recommendations on birth weight z-score once adjusted for race (White and/or Other vs. Black), maternal weight gain during pregnancy (below, meeting, or over IOM recommendation based on pre-pregnancy BMI), maternal height (</≥ 65 in), parity (nulliparous/parous), education (< High School, =High School, > High School), smoking during pregnancy (yes/no), and years of recall (< 4, 4-<6, ≥ 6 yrs).

ACKNOWLEDGEMENTS

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APPENDIX

QUESTIONS FROM THE POUCH FOLLOW-UP SURVEY

Section A. PHYSICAL CHARACTERISTICS:

In this section of the survey we will ask about some physical characteristics, like height and weight.

1. Is your child a: Boy ☐ Girl ☐

2. What is your child's height now? Feet _____Inches _____

3. What is your child's weight now? Pounds _____

4. In your jugment is your child currently: (Please check one)

   Underweight ☐ Normal weight ☐ Overweight ☐

5. What is your height now? Feet _____ Inches_____

6. What is your weight now? Pounds _____

7. How much weight did you gain during the POUCH pregnancy? Pounds _____

Section B. PHYSICAL ACTIVITY:

This section of the survey collects information about your exercise habits both now and during the POUCH pregnancy. We also want to know about how much exercise your child gets, and what kinds of activities he/she chooses. Please answer the following questions as they apply to the time **DURING your POUCH pregnancy**.

1. Did you perform any physical activity in your leisure time during your POUCH Study pregnancy? Yes ❑ No ❑ **If No, Go to 3 below**

If YES:
What was the activity you did the most?_____

On average, how many days a week did you perform this activity? _____ Days per week

On average, how many minutes did you perform this activity? _____ Minutes per day

2. Did you perform a second physical activity in your leisure time during your POUCH Study pregnancy? Yes ❑ No ❑ **If No, Go to 3 below**

If YES:
What was the activity?_____

On average, how many days a week did you perform this activity? _____ Days per week

On average, how many minutes did you perform this activity? _____ Minutes per day

Please answer the following questions as they apply to <u>you</u> **NOW.**

3. Do you **currently** perform any physical activity in your leisure time? Yes ❑ No ❑ **If No, Go to 5 below**

If YES:
What is the activity you do the most?_____

On average, how many days a week do you perform this activity? _____ Days per week

On average, how many minutes do you perform this activity? _____ Minutes per day

4. Do you **currently** perform a second physical activity in your leisure time? Yes ❑ No ❑ **If No, Go to 5 below**

If YES:
What is the activity?_____

On average, how many days a week do you perform this activity? _____ Days per week

On average, how many minutes do you perform this activity? _____ Minutes per day

Please answer the following questions as they apply to your POUCH **<u>Child</u> NOW.**
(Circle <u>one</u> answer that best applies to your child)

5. Compared to other children of the same age and sex, how would you describe your child's level of physical activity?

<u>(Please circle one)</u>

A. Much less than others

B. Somewhat less than others

C. About the same

D. Somewhat more than others

E. Much more than others

6. What does your child usually do when he or she has a choice about how to spend his or her free time? **(Please Circle One)**

1. Almost always chooses sedentary activities, such as watching TV, playing video games, or reading
2. Usually chooses sedentary activities, such as watching TV, playing video games, or reading
3. Just as likely to choose physically active play as inactive recreation
4. Usually chooses physically active play
5. Almost always chooses physically active play

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CHAPTER 4

REVIEW OF LITERATURE PART TWO: CHILD SIZE

INTRODUCTION

Recent results suggest that LTPA during prior to/pregnancy may reduce the odds of giving birth to a LGA infant; however, further effects on child growth and development have not been adequately investigated.[1, 2] Birth size has been directly related to size during childhood and adolescence.[3] Since active women are less likely to have large infants, it is therefore possible that children of more active mothers may also have a reduced risk for being overweight later in life. To date only one study has considered possible influences of maternal LTPA during pregnancy on child size.[4] The authors found that offspring of more active women were lighter and leaner at birth, and had reduced body fatness at five years compared to offspring of less active mothers.[4] However, these results are based on a small sample (n=40) of healthy, middle-class, White women. It has yet to be seen whether LTPA during pregnancy may affect child body size in a more diverse sample with greater power to assess confounding and/or mediation by other perinatal characteristics. Further investigation of the relationships among LTPA during pregnancy, birth size, and child body size has the potential to elucidate a practical intervention to promote healthy pregnancies, birth outcomes, and children with healthy weights.

TERMINOLOGY OF CHILD WEIGHT STATUS

The majority of studies evaluating body size among children have relied on body mass index (BMI) to describe appropriate size rather than body fat measures, which are more difficult to obtain and have no accepted standards for under- or over-fatness. Since

BMI varies considerably with age and maturation, values are usually compared to age- and sex-specific growth charts of a reference population to determine weight status via z-scores or percentile rankings. In the U.S., the Centers for Disease Control and Prevention (CDC) growth charts from 2000 are most commonly used for children ages 2-19 years.[5]

While earlier studies used "at risk for overweight" and "overweight" to designate weight categories, in 2007 an expert committee recommended that the terms "overweight" and "obese" be universally adopted to minimize confusion, provide continuity with adult terminology, and underline the health risk associated with high weight for height status in children.[6] Thus, for the remainder of this dissertation, the term "overweight" will be applied to children with BMI values $\geq 85^{th}$ and $< 95^{th}$ percentile and "obese" will designate BMI values $\geq 95^{th}$ percentile.[6, 7] It should be noted that while BMI classifications among adults are based on risk of disease, risk-related cut-off values for children are not available given that adverse events do not typically occur until adulthood.[7] However, recent evidence on health risks among overweight and obese children suggests that the current cutpoints of the 85^{th} and 95^{th} percentile in BMI are clinically relevant.[8] Furthermore, evidence suggests that the 95^{th} percentile cutpoint for obesity correctly identifies the fattest children with high specificity and moderate sensitivity.[9]

Validity of Parentally Reported Child Body Size Values

The majority of studies on child overweight/obesity rely on parentally and/or self reported height and weight to calculate BMI and/or z-scores. Studies on the accuracy of parental reports of weight, height, and calculated BMI values have shown variable results.[10-14] A study of 864 Dutch children 4 yrs of age found small mean differences

between measured and parentally reported values for weight (-0.02 ± 1.0 and 0.02 ± 1.0 kg for girls and boys, respectively), height (-0.5 ± 1.7 and -0.4 ± 1.7), and calculated BMI (0.1 ± 1.0 for either gender).[14] In total, only 9.7% of children in this study were misclassified on the basis of parental reports into inappropriate weight categories; however, parents were asked to report weight and height values from a recent doctor visit or directly measure the children themselves.[14]

A greater degree of misclassification is evident when mothers are asked to report weight and height of their children without measuring or weighing them. In a different study of 4 yr old weight status, mothers reported weight and height during a face-to-face interview without knowing that measurements would be taken a few weeks later.[10] While no significant height differences were observed, mothers overestimated boys' weights, but not girls', which led to greater overestimation of BMI in boys compared to girls. Despite these errors, 70% of BMI values calculated from maternally reported values were within one standard deviation of measured BMI and kappa statistics indicated fair to moderate agreement for weight status classification by reported and measured values for girls (k=0.337) and boys (k=0.408).[10]

Child age may play a role in the direction and/or magnitude of body size misreport. One study providing information on validity of maternally reported weight and height of Mexican- American children ages 6 mo – 11 yrs demonstrated that mothers tend to *overestimate* weight in young children (<4 yrs) and *underestimate* weight at older ages, while height was underestimated for all age groups.[12] Correlations between reported and measured values were high for heights and weights (r=0.88-0.96) but were low to moderate for BMI (r=0.15-0.44).

The bulk of evidence on the validity of maternal report of child body size indicates moderate to good agreement for individual measures of height or weight, but poorer agreement for calculated BMI values and/or weight classification by BMI.[10, 12, 14] There is some evidence that the accuracy of report is improved when parents are asked to report recent measurements from a health care visit and/or directly measure their child.[13, 14] It appears that maternal misclassification of their children's weight status may be influenced by child gender, with women being more likely to perceive their male children as belonging to a lower weight status category than they really do.[11] Maternal overweight status, child dissatisfaction with their weights, and dieting are also associated with misclassifying overweight children as normal weight at age 14 yrs.[11] In light of these reports, results of studies using parental reports of child height and weight and/or perceptions of child weight classifications should be interpreted cautiously.

EPIDEMIOLOGY OF CHILDHOOD OVERWEIGHT STATUS

Studies from several developed countries have shown marked increases in the prevalence of childhood overweight and obesity in recent years.[15-21] Within the United States, data from national surveys indicate that the prevalence of obesity in children ages 6-11 yrs has increased dramatically from ~6% in the 1970's to ~11% in the 1990's and has continued to rise since then.[22] The most current prevalence values of high BMI among U.S. children are shown in Table 4.1.[23] These values are based on data from the National Health and Nutrition Examination Surveys (NHANES) conducted in 2003-04 and 2005-06 and indicate that prevalence of being overweight and/or obese is higher for older children. No significant differences by gender were seen; however, marked race/ethnic differences in weight status were observed. Specifically, non-Hispanic white

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children have the lowest prevalence of obesity (14.6%) as compared to either non-Hispanic black (20.7%) or Hispanic children (20.9%).[23]

Table 4.1: Prevalence of high BMI for age among US Children, 2003-2006 (Adapted from Ogden et al. 2008)[23]

Age Group (yrs)	N	BMI ≥ 85th Percentile % (SE)	BMI ≥ 95th Percentile % (SE)
2-19	8165	31.9 (1.2)	16.3 (0.9)
2-5	1770	24.4 (1.6)	12.4 (1.0)
6-11	2096	33.3 (2.0)	17.0 (1.3)
12-19	4300	34.1 (1.5)	17.6 (1.2)

Income/socioeconomic status (SES) appears to be weakly and inversely related to child weight status.[20, 22, 24, 25] Data collected from participants in New York's Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) indicate that poverty may be related to obesity rates in young children.[25] Within this state-wide sample of families with income levels ≤ 185% of the federal poverty line, 16.1% of children ages 2-4 years were classified as obese, which is considerably greater than the national average of 12.4% for this age group.[23, 25] Nationwide data indicate weak associations between SES and childhood obesity that are gender and race specific.[26] Using data from multiple waves of NHANES, Wang and Zhang [26] found that SES was unrelated to obesity rates among 2-9 yr old children, while among 10-18 yr olds, high SES was associated with decreased risk of obesity in white boys and girls, but increased risk of obesity among black girls and Mexican American boys. Overall, their results indicate that the increased risk of childhood obesity associated with SES/income is small and appears to be weakening over time.[26]

Unfortunately, not only has the prevalence of obesity among children increased, obese children have also been getting appreciably heavier. When data from the National

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Health Examination Survey (NHES) II or III (1963-1970) are compared to data from the NHANES III (1988-1994), little to no differences in quantile-specific BMI values between the surveys are seen in the lower quantiles, but large differences are present in the higher quantiles, indicating that the heaviest children in NHANES III were significantly heavier than in NHES II or III.[22] Additionally, using estimates of the "extent of overweight" (e.g., the amount by which each obese child exceeds his/her specific BMI cutpoint), obese children were on average 12% heavier than their threshold value in 1971-74, and 14% heavier by 1999-2000.[27] Thus while the prevalence of obesity increased by 182% from 1971-74 to 1999-2000, the extent of overweight increased by 247% according to national data.[27]

HEALTH RISKS OF OVERWEIGHT IN EARLY CHILDHOOD

Short-Term Health Risks

Childhood overweight/obesity is associated with both short- and long-term health risks. In fact, many obesity-related health conditions once noted among adults only are increasingly being diagnosed among children and adolescents.[28] Specifically, obese children have been shown to be at increased risk for concomitant hypertension/high blood pressure, abnormal enthothelial function, insulin resistance and/or type II diabetes, dyslipidemia, and even atherosclerosis.[8, 28] The emergence of childhood type II diabetes in particular appears to have paralleled the increasing prevalence of obesity and the two may be causally linked.[28, 29]

Authors have also noted a clustering of risk factors among overweight children, commonly termed the metabolic syndrome.[8, 28] The metabolic syndrome is broadly defined by the presence of abdominal obesity, elevated blood pressure, glucose, and

triglycerides, and lowered high-density lipoprotein-cholesterol (HDL-C).[30] Specific cutpoint criteria for each risk factor in children are not standardized, thus true prevalence rates are difficult to estimate. However, it appears that between 4-10% of adolescents in the U.S. have the metabolic syndrome and the prevalence increases to 30-50% among obese children/adolescents.[30] It is important to note that children do not have to be obese to be at increased risk for metabolic syndrome components. Bell et al.[31] have reported continuous relationships between increasing BMI z-score and blood pressure and fasting insulin, as well as curvilinear relationships with HDL-C and triglycerides such that changes in BMI z-score at the high end of the spectrum had a greater impact on unfavorable lipid profiles. These results, based on a sample of only 177 children, indicate that children's risks of cardiovascular/metabolic complications increase across the range of BMI and are not threshold-dependent.[31] In addition to cardiovascular/metabolic co-morbidities of overweight/obesity, reviews of past literature have also noted increased prevalence of psychological problems such as depression and anxiety (especially among girls), asthma, and gastroesophageal reflux associated with overweight status.[8, 28]

Long-Term Health Risks

Perhaps even more troubling than the short-term health consequences, childhood overweight/obesity appears to track into adulthood, thereby placing these children at higher risk for adult obesity and obesity-related health conditions. Two recent reviews of both U.S. and European studies found strong evidence for the persistence of childhood overweight/obesity into adulthood, which was significantly more likely among children with at least one overweight parent, with more severe overweight status, and/or with overweight/obesity present at older ages.[8, 32] While risk estimates varied considerably

among studies, overweight children were at least twice as likely as their normal weight peers to become overweight adults (OR/RR ranged from 1.9 to 22.3 for overweight children >2 yrs of age).[32] Childhood overweight/obesity is also linked to increased risk of obesity-related health conditions in adulthood, such as cardiovascular disease and diabetes.[8, 33, 34]

Beyond the mere presence of overweight/obesity in childhood, rapid growth during "critical time periods" appears to confer greater risk for future adverse health outcomes.[35] Researchers are just now beginning to explore the individual contributions of rapid growth during infancy, the timing of the adiposity rebound in childhood (i.e. the nadir of BMI or weight), and the phenomenon of changing BMI percentile growth trajectories towards risk of later obesity.[24, 35, 36] Thus far, results indicate that factors operating in infancy and early childhood may have dramatic influences on future weight status.[24, 36] In particular, rapid growth during infancy resulting in changing growth trajectories and/or reaching the nadir of weight or BMI (e.g. hitting the "adiposity rebound") earlier in childhood have been significantly associated with increased risk of adolescent/adult obesity.[24, 36-38] Given both the short-term and long-term health consequences of childhood obesity, it is important to identify early factors which predispose children towards overweight/obesity for the purposes of intervention/prevention strategies.

CHILD BEHAVIORS AND CHILD BODY SIZE

The causes of childhood overweight/obesity are multifaceted and complex. This dissertation focuses primarily on perinatal exposures that may influence child growth and body size; however, child behaviors and parental influences must also be considered.

More proximal exposures, such as child behaviors and parental characteristics, will be briefly reviewed before considering the impact of more distal perinatal factors on child overweight/obesity in greater detail.

Child Physical Activity

Any investigation of factors related to child weight status must consider the influence of the child's own behaviors. Intuitively, the emergence of childhood overweight would seem to be primarily a problem of energy balance. Either the child is consuming too much energy or is not expending enough energy to experience normal growth patterns and is thus storing excess fat and becoming overweight. While this argument seems logical, it probably oversimplifies the relationships among LTPA, diet and weight status in childhood. In fact, while research supports relationships between a child's LTPA participation and his/her weight status, results have been neither as strong, nor as consistent as expected.[39]

National guidelines recommend that children participate in at least 60 min/day of at least moderate LTPA.[40] U.S. youth participation in LTPA varies by age with 42.0% of 6-11 yr olds meeting recommendations, but only 8.0% of 12-15 yr olds and 7.6% of 16-19 yr olds meeting recommendations.[41] Gender differences are also seen with fewer girls meeting recommendations than boys at any age group (35% vs. 48% and 3% vs. 12% for girls vs. boys at ages 6-11 and 12-15 yrs, respectively).[41] These prevalence rates are based on accelerometry data from the 2003-04 NHANES, and thus provide an objective assessment of LTPA participation in a national sample of children.

One of the major difficulties in synthesizing results of past research on LTPA and body size in children is the wide array of methodologies employed to measure LTPA.

These have ranged from subjective measures such as parental/caregiver report and direct observation to the more objective accelerometry and/or doubly labeled water techniques. Reviews on the impact of LTPA on risk of childhood obesity have noted that much inconsistency among previous studies may be attributed to variation in LTPA measurement methods.[39, 42, 43] Despite these obstacles, most studies report negative correlations between LTPA and fatness among children; however, results with BMI tend to be null.[44-51]

Among a representative sample of 3-year-old children, obesity prevalence did not vary by outdoor play time or by minutes/day of TV viewing.[51] However, Trost et al. found that overweight 3-5 yr old boys were significantly less active than non-overweight boys.[46] Trost et al. employed more exact measures of LTPA, including direct observation and accelerometry, which may have resulted in greater power to detect differences by overweight status. Interestingly, no significant differences in LTPA were observed between overweight/non-overweight girls.[46] The authors speculated that this may have been due to girls choosing to participate in less vigorous activities that were not as influenced by obesity status. Results from a study of somewhat older children (6-8 yrs) showed that neither free-living activity energy expenditure nor LTPA level calculated from 7-day doubly labeled water were significantly related to BMI; however inverse relationships with fat mass index were noted (beta coefficient = -5.57, $p<0.001$).[48] Abbott and Davies also found LTPA level from doubly labeled water to be inversely related to percent body fat in 5-10.5 yr old children ($r= -0.44$, $p=0.004$).[47]

The directionality of the relationship between overweight status/body fatness and LTPA participation could not be established by the previously mentioned studies due to

the cross-sectional nature of these data. Longitudinal data from the Framingham Children's Study, however, indicate that LTPA in early childhood results in smaller gains in BMI, triceps, and sum of five skinfolds.[45] After controlling for child gender, baseline age and BMI, TV watching, percentage of calories from fat, and baseline BMI and education level of both parents, the most active children had significantly lower triceps and sum of skinfolds at the end of follow-up.[45] A trend for lower BMI among the most active tertile was also observed; however, this did not reach statistical significance (BMI = 20.3 ± 0.6, 19.8 ± 0.5, and 18.6 ± 0.6 kg/m^2 for low, moderate, and high active tertiles, respectively, p=0.052).[45]

Unfortunately, LTPA intervention/prevention studies have not been able to demonstrate measureable improvements in weight status to date. A recent review of school-based obesity prevention programs concluded that changes in diet and/or LTPA did not lead to improvements in overweight outcomes, but emphasized that methodological quality of these trials was low.[52] A systematic review of three long term (>1 yr) and four short term (3 mo – 1 yr) interventions for preventing obesity also found inconclusive evidence for child LTPA exerting a protective effect.[43] However, a third review on interventions to reduce sedentary behaviors found consistent evidence for improved weight indices associated with fewer hours/wk of sedentary activity.[53] It is possible that sedentary time (e.g., time spent watching TV or playing video games) is easier to measure and/or more susceptible to intervention efforts, thus greater affects on weight status are able to be demonstrated as compared to LTPA interventional efforts.

It is difficult to know the mechanism through which sedentary behavior may be related to weight status. One study of ~1000 young children found that 2+ hrs/d of TV

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time was associated with increased risk of being overweight at 3 yrs (OR=2.92, 95%CI: 1.36-6.24) and 4.5 yrs (OR=1.71, 95%CI: 1.03-2.83).[54] However, once adjusted for sex, race, maternal education, marital status, and age, TV exposure was no longer a significant predictor of overweight status.[54] Thus, the relationship between sedentary time and child overweight status may be confounded by other family and lifestyle factors that travel with more sedentary behavior. It is also possible that sedentary behavior increases risk of overweight/obesity through displacing LTPA, increasing energy intake via snacking, effects of food advertising on TV, and/or decreased metabolic rate during sedentary time.[53] Regardless of the mechanism involved, in recognition of the health risks associated with excess sedentary behavior, the American Academy of Pediatrics has recommended that screen time be restricted to 60 minutes or less per day.[55]

Child Dietary Patterns

In addition to energy expenditure via LTPA (or the lack thereof), energy intake/dietary habits have also been examined in relation to risk of childhood overweight/obesity. Dietary recommendations vary by age and gender among children; however, the most recent guidelines published by the American Heart Association stress that children >2 yrs old should limit juice intake, eat fruits and vegetables daily, focus on whole-grain breads and cereals, reduce intake of sugar-sweetened foods and beverages, and seek to balance dietary calories with LTPA to maintain normal growth.[56] National data indicate that mean energy intake among children has not changed significantly since the late 1970's, except among adolescent females who demonstrated a significant increase in energy intake from the 1970's to 1988-94.[57]

To date, studies on the importance of dietary factors on child weight status have been inconclusive. Cross-sectional studies have failed to demonstrate significant relationships between either global energy consumption or specific dietary elements and child BMI or fatness.[58] Similarly, longitudinal studies in children have not demonstrated relationships between energy intake or percentage of macronutrient consumption and rates of weight gain or future risk of overweight.[58] Studies focusing on consumption of sugar-sweetened soft drinks and child weight status have also had limited success. More than half the studies with cross-sectional data reported null associations and only 8 of 16 longitudinal studies showed any significant relationships between sweetened drinks and weight gain, which were apparent in only select subgroups and/or disappeared with adjustment for confounders.[59]

Inconsistencies in methodologies for assessing dietary patterns, definitions of meeting guidelines, and a predominance of cross-sectional data may be obscuring true relationships between dietary patterns and risk of childhood obesity.[58, 59] For example, under-reporting of food-consumption is a problem that may vary by child weight status, with more obese children underestimating dietary intake the most.[60] Also children who are currently overweight/obese may be restricting calories to lose weight, thereby disguising differences in macronutrient consumption between children who maintain healthy weights and those who become obese. More research is needed with better measures of dietary quality among children of all age ranges to further investigate relationships between dietary factors and weight status.

Recently, milk consumption in childhood has received marked attention as a possible risk factor for the development of overweight/obesity. Significant inverse

relationships between frequency of milk consumption and child size have been reported among cross-sectional samples.[61] The mechanism linking milk consumption to weight status is currently unclear, although the association was significant even after adjustment for a range of confounding variables including parental weight status and education, child LTPA, age, gender, and frequency of consumption of other foods.[61] Longitudinal research on milk consumption is needed to determine the directionality of its relationship with child obesity.

Summary of Child Behaviors and Weight Status

In conclusion, evidence for significant relationships between LTPA or dietary patterns and child weight status is modest, although studies utilizing objective measures of LTPA have shown significant inverse relationships with body fatness measures.[39] Excessive sedentary behavior has also been shown to be a consistent risk factor for overweight/obesity.[53] While the majority of dietary evidence has been weak, inverse associations between BMI z-scores and frequency of milk consumption among children have been observed.[61] Further research on child behaviors is needed to determine viable avenues for prevention of overweight status. When examining the influences of child LTPA and dietary behaviors on child weight status it will also be important to consider parental characteristics that may modify the child's susceptibility for overweight status and/or influence the child's probability of participating in healthy behaviors.

PARENTAL CHARACTERISTICS AND CHILD BODY SIZE

Studies of parental influences on child weight status have focused mainly on the concurrent presence of parental overweight/obesity and parental influences on child dietary and LTPA behaviors. Both maternal and paternal size are positively related to

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child size [50, 62] and parental overweight/obesity significantly increases risk for child obesity.[62-64] A study of over 2000 children found that odds of obesity at 4.5 yrs of age were significantly higher among children with one (OR=2.1, 95%CI: 1.3-3.6) or two (OR=3.2, 95% CI: 1.7-5.8) currently overweight parents compared to children of normal weight parents.[63] These results have been replicated in other samples with a variety of child age groups.[50, 62, 64]

The mechanism for the relationship between parental and offspring weight status has not been established. Genetic influences are undoubtedly at play; however, parental overweight status may also affect child weight through alternate environmental pathways. Results from classic studies conducted by Claude Bouchard in the 1980's indicate that heritability of fat mass in adults reaches ~25% of the phenotypic variance, while family studies indicate that the maximum heritability of obesity phenotypes ranges from 30-50%.[65, 66] A more recent study of Hispanic children found heritability of anthropometric measures to range from 31-71%, with height having the strongest heritability (71%) and weight and fat mass having comparable heritabilities of 36% and 33%, respectively.[67] Thus children of obese parents are at increased risk of overweight/obesity due to their genetic make-ups.

In addition to genetic influences, parental obesity may affect child weight status through the creation of an "obesogenic" environment at home that de-emphasizes LTPA opportunities and increases access to energy-dense foods. Parental dietary and LTPA patterns are known to influence children's participation in healthy behaviors.[68, 69] Within the Framingham Children's Study, 7 yr olds with two active parents were 5.8 times more likely (95%CI: 1.9-17.4) to be active themselves compared to children with two inactive

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parents.[69] Young children are also dependent upon parents to provide access to nutritious food and to set appropriate serving sizes. Parental monitoring and family cohesion have been significantly related to youth healthy eating behaviors and LTPA participation.[68] A recent review of child feeding behaviors concluded that parental monitoring of fat intake predicted lower child BMI, but that both maternal pressure to eat and maternal restriction of foods were associated with higher weight gain throughout childhood.[70]

It should be noted that ethnic and cultural differences in adult obesity rates, child feeding practices, and LTPA promotion may be partly responsible for the higher prevalence of obesity among African American and Hispanic children, as compared to White children. It is known that overweight/obesity is more prevalent among African American and Hispanic adults compared to Whites, thus minority children have a higher probability of having at least one overweight/obese parent.[71] A recent review demonstrated that African American and Hispanic children also reported higher levels of obesity promoting behaviors such as skipping breakfast, eating fast food, ingesting low amounts of fruits and vegetables, and frequent TV watching.[72] Additionally, parental perceptions/concern about child weight status may differ by race/ethnicity due to alternate cultural norms which may be more permissive of obesity.[72]

Summary of Parental Influences and Child Weight

In conclusion, children with an overweight parent are more likely to be overweight themselves.[63] The mechanism through which parental obesity confers risk for child obesity is multifaceted, including both genetic and environmental influences.[24] The presence of maternal obesity has sometimes been shown to have a greater affect on child obesity than paternal obesity.[73] It is possible that maternal obesity may confer additional

risks to the offspring via changes in the prenatal environment which influence fetal development.[3, 74]

PERINATAL EXPOSURES AND CHILD BODY SIZE

Given the increased prevalence of obesity among young children, researchers have begun to examine early life and prenatal exposures in relation to child growth and body size.[71, 75] Due to our inability to directly measure fetal exposures, birth weight has often been used as an indicator of prenatal environmental conditions.[76] Other perinatal factors that have received attention as potential risk factors for childhood obesity include maternal size during pregnancy and gestational weight gain, the presence of health conditions during pregnancy such as diabetes, maternal behaviors during pregnancy such as smoking, nutrition, and LTPA, and factors operating during infancy including infant growth rates and breastfeeding practices. Each of these factors will now be reviewed for relation to child size and body composition.

Birth Weight and Child Size

Past research has demonstrated either a linear or J- / U-shaped relationship between birth weight and subsequent child BMI.[3, 74, 76, 77] Overall, macrosomic/LGA infants have approximately twice the risk of becoming overweight children as compared to normal weight infants.[63, 74, 76] Low birth weight combined with rapid growth during infancy has also been consistently associated with risk of overweight and central adiposity in childhood.[3, 77]

When considering body composition specifically, birth weight has shown strong direct relationships with fat-free mass, but correlations with future fat mass/percent fat have been less consistently demonstrated.[76] LGA/macrosomic infants have been found to

have increased body fatness at birth when compared to normal weight infants. [78-80] Some have also shown that excess fat mass persists into early childhood, placing these children at higher risk of overweight/overfatness and the metabolic syndrome.[81-83] However, while absolute amounts of body fat may be higher among children born macrosomic/LGA, lean body mass is also higher when compared to normal weight children, thus relative percent fatness may be unchanged.[76, 84] To date, results among past literature are mixed, with some studies reporting direct relationships[81, 85] and others finding either no relationship or inverse relationships between birth weight and measures of fatness in childhood.[38, 86-89] Differing methodologies for assessing body composition, the inclusion of variable child age ranges, and racial/ethnic variations in maturation and body fat distribution make it difficult to draw conclusions based on the small number of studies that have been conducted thus far. Therefore, while birth weight has been shown to be directly related to child weight and BMI, effects on individual components of body size are less certain.[38, 76]

The mechanism linking birth weight to child body size is not clearly understood. It is possible that birth weight mediates prenatal exposure effects on future child size. In this scenario, size at birth merely marks an adverse prenatal environment that sets the stage for later obesity. Hypothesized prenatal exposures have included maternal obesity and/or inappropriate weight gain during pregnancy (with or without the presence of diabetes), as well as maternal behaviors during pregnancy such as smoking, nutrition, and LTPA.

Maternal Size / Weight Gain during Pregnancy and Child Size

In Chapter Two it was shown that maternal size and weight gain during pregnancy were both positively related to birth weight, with the largest infants born to

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overweight women who gained excess weight.[78, 90] Additionally, maternal overweight status is associated with greater neonatal fat mass, even when overall BW is unaffected.[91] It now appears that maternal size and gestational weight gain may have lingering effects on offspring size and fatness during childhood as well.[74, 92, 93]

Studies have consistently demonstrated increased risk for overweight/obesity and excess body fatness among offspring of women who were overweight/obese during pregnancy.[74, 77, 92-94] Relative risk of offspring obesity at 2-4 yrs is twice as high among children whose mothers were obese during pregnancy, even when controlling for birth weight, gender, maternal demographics, smoking, and gestational weight gain (RR= 2.0-2.3 depending on child age).[94] Among older children, pre-pregnancy BMI has also been positively associated with child adiposity and weight on a continuous scale.[92] After controlling for child age, birth weight, infant weight gain, breastfeeding duration, maternal height, gestational weight gain, and smoking during pregnancy, maternal mid-arm circumference in late pregnancy and pre-pregnant BMI were each significantly related to higher offspring fat mass index (fat mass (kg)/ height $(m)^{4.49}$) , but not lean mass index (lean mass (kg)/ height $(m)^{2.2}$) at 9 yrs of age.[92]

There are several pathways through which maternal obesity during pregnancy may influence later child weight status. These include genetic contributions and the encouragement of unhealthy dietary and LTPA patterns as discussed previously. In addition, the presence of maternal obesity may alter the prenatal environment, thereby signaling changes in fetal development that promotes excess weight gain/fat storage later in life.[35] Animal models have shown that offspring of overweight rodents overfed a high-fat diet during pregnancy experienced altered pancreatic development and displayed

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increased adiposity in adulthood.[35] Additionally, increased nutrient supply during pregnancy has been shown to enhance adipogenesis and increased fat deposits in pig and sheep offspring.[35]These results indicate that fetal over-nutrition, frequently present among obese women, may alter regulatory pathways for energy homeostasis in the offspring and increase risk of obesity independently from postnatal environmental influences.

Excessive gestational weight gain has also been related to child overweight/obesity; however, the significance of this relationship has sometimes been altered by controlling for maternal pre-pregnant size.[92, 93, 95, 96] When compared to inadequate weight gain (based on IOM recommendations and pre-pregnancy BMI), excessive weight gain is associated with higher BMI z-scores and more than 4 times the risk of overweight at 3 yrs of age (OR=4.35, 95%CI: 1.69-11.24).[95] In contrast, another study found no evidence of a significant main effect for gestational weight gain on offspring obesity at 3 yrs; however a significant interaction between maternal BMI and gestational weight gain was noted such that the risk of obesity was highest among offspring of obese women who gained excess weight.[96] In general, it appears that the presence of maternal obesity is more important than excess weight gain for the development of childhood overweight/obesity.[74, 93]

Maternal Diabetes in Pregnancy and Child Size

Diabetes present during pregnancy is known to increase size at birth and is also associated with increased risk of child obesity.[83] In a study of discordant sibships among a sample of Pima Indians, Dabelea et al.[97] showed that mean BMI was 2.6 kg/m^2 higher among offspring of diabetic vs non-diabetic pregnancies. This study involved 183

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siblings from 52 families and compared offspring BMI within a 3-yr time interval (i.e., 6-<9 yrs, 9-<12 yrs). Because siblings shared similar postnatal environments and received similar genetic influences on body size, these results suggest that exposure to the intrauterine diabetic environment specifically increases risk of childhood obesity.[97] Other studies involving larger, nationally representative samples of children and families have found that the relationship between gestational diabetes and risk of offspring obesity is attenuated after controlling for maternal BMI.[83, 98] Complex interactions among maternal obesity, gestational diabetes, and size at birth (i.e., LGA) are likely to exist, and teasing apart the individual contributions of each factor towards child body size is difficult.[82] It is possible that shared maternal/child environments which contribute towards maternal weight and gestational diabetes also promote excess weight gain in the offspring and therefore cloud relationships between fetal exposure to diabetes and future obesity.

Mechanistically, both maternal obesity and/or diabetes during pregnancy (either pre-gestational or of gestational onset) would increase the delivery of glucose, lipids, and amino acids to the fetus, leading to increased fetal growth and larger infant fat mass.[74, 99, 100] Animal studies further support fetal over-nutrition altering offspring metabolic processes leading to increased fat storage.[35] In utero exposure to diabetes among rats has been shown to alter appetite control among offspring as well leading to hyperphagia and overweight later in life.[3] Overall, studies support an association between gestational diabetes and offspring obesity; however, separating the individual effects of diabetes, maternal obesity, and excess gestational weight gain is difficult.[77]

Maternal Smoking during Pregnancy and Child Size

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Beyond maternal anthropometrics and health conditions during pregnancy, maternal behaviors may also alter the fetal environment, leading to downstream effects on child body size. Specifically, the impacts of maternal smoking, energy intake, and LTPA during pregnancy have been considered in relation to size at birth and in childhood.

Studies have consistently reported a significant association between prenatal smoking and risk of childhood overweight.[77, 101] Regardless of the methods employed to measure prenatal smoking, effect sizes for the odds of child overweight/obesity have ranged from ~1.3 to 3.0, with most studies showing modest relationships (e.g. OR's = 1.5-2.0).[64, 93, 101, 102] Data from the Pregnancy Nutrition Surveillance System and the Pediatric Nutrition Surveillance System covering 9 US states and 2 tribal nations indicate that the effect of maternal smoking on offspring obesity may be modified by race/ethnicity.[103] In this study, smoking during pregnancy was associated with increased risk of child obesity at 2-4 yrs of age among Non-Hispanic White (OR=1.42, 95%CI: 1.34-1.50) and Non-Hispanic Black (OR=1.19, 95%CI: 1.05-1.35) children, but not among Hispanics, Native Americans, or Asians.[103] Dubois et al[63] also noted a significant interaction between smoking during pregnancy and infant weight gain such that children born to smoking mothers who were macrosomic and experienced the highest rate of infant growth were at similarly high risk of obesity at 4.5 yrs as were children born to smoking mothers with normal birth weight who also experienced the highest rate of infant weight gain.

The biological mechanism linking smoking to later obesity is unclear. It has been hypothesized that maternal smoking leads to fetal undernutrition due to uteroplacental

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vasoconstriction, which is followed by excessive "catch-up" growth postnatally.[77, 101] Alternatively, carbon monoxide associated with maternal smoking may affect fetal oxidative metabolism, thereby imprinting metabolic pathways and leading to differential patterns of fat metabolism/storage in the offspring.[77, 101] Aside from these biological explanations, it is also possible that maternal smoking simply marks the presence of other disadvantageous maternal behaviors/characteristics such as maternal under- or overweight and/or poor maternal nutrition. However, studies which have controlled for logical confounding factors have demonstrated a persistent, if modest, relationship between smoking during pregnancy and larger offspring size in childhood.[101]

Maternal Nutrition during Pregnancy and Child Size

Fetal fuel supply is a key determinant of birth weight and appears to alter programming of metabolic pathways, thereby influencing future offspring body size/composition. The consequences of fetal *over-nutrition*, as evident in the presence of maternal diabetes and/or obesity during pregnancy, have been outlined above. The strongest evidence for a lasting impact of fetal *under-nutrition* comes from follow-up studies on the Dutch Famine cohort. Among 19-yr old men, risk of obesity was significantly higher among those exposed to famine conditions in the 1st or 2nd trimester (OR=1.94, 95%CI: 1.54-2.44), but significantly lower among those exposed only in the 3rd trimester (OR=0.62, 95%CI: 0.44-0.86).[104] These results indicate that the timing of alterations in maternal nutrition may have important consequences in terms of offspring risk for obesity.

Past research has focused on the extremes of maternal nutrition (under- or over-nutrition) and offspring outcomes.[24, 38, 101] Studies on maternal dietary

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quality/composition during pregnancy and child health have been few with mixed results.[105] More research with detailed measures of energy consumption and dietary quality throughout pregnancy are needed to more fully understand the effects of maternal nutrition on offspring health throughout the normal range of dietary habits, as well as the extremes. From the available data, it appears that variations to maternal energy consumption within the normal range do not influence future child weight status.[38]

Maternal Physical Activity during Pregnancy and Child Size

To our knowledge, only one investigator has examined the relationship between maternal LTPA during pregnancy and child body size. James Clapp, MD examined body size and neurodevelopmental outcomes at 5 yrs of age among offspring of women who had either vigorously exercised both before and throughout pregnancy (n=20) or had regularly exercised pre-pregnancy but voluntarily stopped activity during pregnancy (n=20).[4] In an attempt to isolate the effects of LTPA on offspring outcomes, participants in this case-control study were matched based on prenatal factors including maternal smoking status, income, education, marital status, parity, occupation, preconceptional fitness and LTPA participation, and maternal/paternal weight, height, and body fatness; and postnatal factors including breastfeeding duration, type of child care, parental LTPA participation post-pregnancy, postnatal maternal change in weight, child gender, gestational age at delivery, clinically normal growth patterns in the first year, absence of serious illness, and number of new siblings. This approach resulted in a highly select sample of women, but eliminated the need for adjusted analyses. Maternal exercise was measured prospectively throughout pregnancy, birth weight and fatness (tricep and subscapular skinfold thicknesses) were assessed by a trained investigator within 2 hours

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of birth, and weight, height, and skinfolds (triceps, subscapular, suprailliac, abdominal, and mid-thigh) were re-assessed within 1 month of each child's 5 yr birthday.

Results demonstrated that offspring of women who exercised throughout pregnancy were significantly lighter (BW= 3.4 ± 8.0 v. 3.6 ± 7.0 kg, p=0.01) and leaner (%fat= 10.5 ± 0.9 vs. 15.1 ± 0.6, p=0.01) at birth compared to the control group.[4] Offspring in the exercise group remained lighter (weight=18.0 ±0.5 vs. 19.5 ±0.6 kg, p=0.01)) and leaner (Sum of 5 skinfolds = 37 ± 1 vs. 44 ± 2 mm, p=0.01) at 5 yrs of age as well. These results provide preliminary support that LTPA during pregnancy may have lasting effects on child body size; however, the mechanism of effect is unclear.

Our lab is currently conducting a pilot study following up women whose LTPA was carefully measured during pregnancy to determine possible relationships with child health outcomes at 8-10 yrs.[106] Preliminary data analyses on 20 mother/child pairs indicate that LTPA later in pregnancy tended to be inversely associated with child BMI (r_s= -0.40, p=0.08; r_s= -0.41, p=0.07 for the 2nd and 3rd trimesters, respectively) and with child waist circumference (r_s= -0.45, p=0.05; r_s= -0.43, p=0.06 for the 2nd and 3rd trimesters, respectively). No significant associations among LTPA during pregnancy and child percent body fat were noted; however, pre-pregnancy LTPA was inversely associated with child percent body fat (r_s= -0.60, p=0.005). Future studies including larger and more diverse populations are needed to confirm these findings and begin to unravel the biological pathway involved.

Investigating the effect of LTPA during pregnancy on child body size requires careful consideration of potentially confounding or modifying factors. As we have seen, maternal obesity, high pregnancy weight gain, and diabetes during pregnancy all increase

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risk for high BW and childhood overweight status.[63, 74, 94] Additionally, current LTPA levels of children are inversely associated with body fatness ($r = -0.52$, $p<0.01$)[49] and active children gain significantly less body fat between 3-5 years of age compared to inactive children.[44] Thus, the possible impact of maternal LTPA on child body size should be evaluated in light of the current activity level of the child as well as descriptive information on maternal body size and pregnancy conditions.

Breastfeeding and Child Body Size

In addition to the prenatal exposures outlines above, much research interest has been paid to the possible effects of infant feeding practices on future child weight status. The American Academy of Pediatrics recommend exclusive breastfeeding for the first six months of life and support breastfeeding for the first year and beyond when possible.[107] While breastfeeding is known to confer several health benefits to the infant, associations between breastfeeding and future risk of obesity have shown contradictory results. Several cohort studies have noted small protective effects of breastfeeding on the risk of childhood obesity;[108-110] however, others have reported null findings.[64, 77, 111-113] Recently, quantile regression analyses has demonstrated that breastfeeding had a larger effect of lowering BMI above the 90th percentile of the BMI distribution among children 5-7 years old.[109] While these findings require confirmation, they suggest that the protective effect of breastfeeding on childhood obesity may not always be demonstrated because it is limited to the upper parts of the BMI distribution.

Duration of breastfeeding appears to show dose-response relationships with obesity risk, with studies showing that infants breastfed more than 4 or 6 mo had lower risk of obesity than those breastfed for a shorter time or not at all.[24, 108] Unfortunately,

previous studies have rarely accounted for other maternal factors that may influence associations between breastfeeding and childhood obesity, such as smoking, obesity, and socioeconomic status, and none have considered the impact of interim dietary and LTPA behaviors of the child.[24] Those studies which have included maternal size along with breastfeeding have noted that maternal BMI and/or overweight status is a stronger risk factor for childhood obesity than is breastfeeding.[111, 114]

It has been hypothesized that breastfeeding improves the child's ability to self-regulate dietary intake, while the rapid weight gain associated with formula feeding in early infancy confers added risk of future obesity. It also appears that breastfeeding may alter future maternal feeding patterns. In particular, women who breastfed 12 months or longer demonstrated lower levels of control over food choices and frequency of eating and were more responsive to hunger/satiation cues from their toddlers when compared to women whose infants were formula fed.[115, 116] Thus, breastfeeding may have indirect influences on child obesity via changes to maternal and child food intake behaviors. Overall, it appears that breastfeeding offers some protection against later child obesity; however other perinatal factors including maternal size and infant growth rates appear to have larger influences on child growth and body size.

SUMMARY

Converging lines of epidemiological and animal study evidence support the roles of both genetic and postnatal environmental factors on the risk of childhood obesity, as well as prenatal exposures. Causal links between perinatal exposures and future risk of childhood overweight/obesity are beginning to be established. Prospective cohort studies on exposures occurring prenatally and in early infancy have demonstrated clear temporal

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relationships without reliance on recalled data which may be biased.[101] For some exposures such as maternal diabetes, obesity during pregnancy, and excessive gestational weight gain, animal studies have shown biologically plausible pathways between alterations to fetal nutrition and changes to metabolic pathways which set the stage for offspring obesity.[35] Biological mechanisms are less clear for exposures such as maternal smoking and/or LTPA during pregnancy to directly impact child weight status. The third causal criteria of consistency of findings has been demonstrated across age-ranges and populations for child weight status to be associated with maternal overweight and/or diabetes during pregnancy, excessive gestational weight gain, smoking during pregnancy, and breastfeeding with few exceptions.[3, 74, 77] Consistency has not been demonstrated for maternal LTPA during pregnancy as only one study has yet examined this topic.[4]

Some factors, such as maternal smoking and breastfeeding have also demonstrated dose-response relationships with future child size. However, the strength of association for perinatal factors has varied, with most showing modest associations and maternal overweight/obesity demonstrating the strongest effect on child obesity.[101] Findings for these perinatal exposures appear to demonstrate a high degree of coherence with existing theory and knowledge; however, unfortunately studies have varied in their attention to confounding factors. Thus alternative explanations, including the existence of a common environment that led to both the exposure (e.g., maternal obesity) and the outcome of child obesity cannot be ignored.[101]

In total, the perinatal factors reviewed here fulfill the majority of causal criteria for relationship to child overweight/obesity status; however, more work is needed to

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refine biological pathways while controlling for important confounding variables. Particularly, LTPA during pregnancy deserves more attention as a possible avenue to improve the health of the mother while also possibly decreasing risk of the child becoming overweight later in life.

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CHAPTER 5:

MATERNAL PHYSICAL ACTIVITY DURING PREGNANCY, CHILD SEDENTARY BEHAVIOR, AND CHILD WEIGHT STATUS

ABSTRACT

Purpose: To evaluate the effects of maternal leisure-time physical activity (LTPA) during pregnancy and child sedentary behavior on child weight status at 3-9 years. **Methods:** Women enrolled in the Pregnancy Outcomes and Community Health Study (1998-2004) were studied again in 2007. Follow-up efforts were extensive for a subcohort and minimal for the remainder, or non-subcohort. Original data collection provided maternal demographics and birth outcomes. At follow-up women reported child height and weight (used to calculate body mass index (BMI)), child leisure-time behavior (sedentary, some sedentary/some active, or active), and recalled pregnancy LTPA. Women were classified as inactive (reference category), insufficiently active, or meeting LTPA recommendations. A four-category maternal/child LTPA variable was created (reference: any LTPA during pregnancy and non-sedentary child leisure-time behavior). Children were classified as healthy weight (5-<85th), overweight (85-<95th), or obese (≥95th) based on age- and sex-specific percentiles. **Results:** Among the non-subcohort, LTPA during pregnancy were associated with borderline significant reduced odds of child overweight and obese status by approximately 50%. Among the subcohort, LTPA during pregnancy significantly increased odds of child overweight (aOR= 1.9 and 2.1 for insufficient activity and meeting LTPA recommendations) but non-significantly decreased odds of obesity (aOR=0.7 for both insufficient activity and meeting LTPA recommendations). Maternal inactivity during pregnancy combined with sedentary child

behavior tended to increase odds of obesity within both the non-subcohort (aOR=2.5, 95%CI: 0.8-7.4) and subcohort (aOR=1.8, 95%CI: 0.8, 3.7). **Conclusion:** Maternal LTPA during pregnancy may have a lasting effect of reducing risk of child obesity, even when considering their children's own sedentary behavior.

INTRODUCTION

The prevalence of childhood obesity in the U.S. has increased steadily since the 1970's, with current values indicating that 16% of U.S. children ages 2-19 yrs are obese (i.e., age and sex-specific body mass index (BMI) $\geq$ the 95th percentile).[1, 2] Childhood obesity is associated with increased risk of concomitant high blood pressure, insulin resistance, and dyslipidemia, as well as risk for adult obesity and cardiovascular disease.[3-5] Thus for the current and future health of youth, it is imperative to determine modifiable risk factors for childhood obesity to aid prevention and/or intervention efforts.

While the causes of childhood obesity are multifaceted and complex, prenatal exposures are increasingly being examined in relation to future child size. Maternal overweight/obese status during pregnancy, excess gestational weight gain, gestational diabetes, smoking during pregnancy, and extreme birth weight (low or high) have each been associated with an increased risk for child obesity or excess fatness.[6-10] One case-control study has also demonstrated that offspring of women who remained sedentary throughout pregnancy had increased body fat at five years of age when compared to offspring of women who exercised throughout pregnancy.[11] These results suggest that maternal leisure-time physical activity (LTPA) during pregnancy may reduce offspring susceptibility for excess fat storage. However, this study was based on a small select sample and did not consider the impact of the children's LTPA levels.

Despite differing measurement methods, past studies have shown child LTPA participation to be inversely associated with body size, including body fatness.[12-14] In addition, longitudinal data support the hypothesis that LTPA in early childhood results in lower BMI and body fatness later in childhood.[15] However, studies examining the

relationship between child LTPA participation and body size have rarely considered prenatal exposures, and none have evaluated possible influences of maternal LTPA during pregnancy.

The purpose of this study, therefore, was to evaluate the separate and combined effects of maternal participation in LTPA during pregnancy and children's leisure-time behavior on child weight status at 3-9 years of age. We hypothesized that LTPA during pregnancy would be associated with reduced odds of child overweight and obese status. We also hypothesized that children who engage in mostly sedentary leisure-time activities and whose mothers were inactive during pregnancy would have the highest risk for being classified overweight or obese when compared to children who choose non-sedentary leisure-time activities and whose mothers were active during pregnancy.

METHODS

Study Population

Participants in this study were enrolled in the Pregnancy Outcomes and Community Health (POUCH) Study. The POUCH study originally recruited women in gestational weeks 15-27 from 1998-2004 from 52 clinics in five Michigan communities. Inclusion criteria were singleton pregnancy with no known congenital anomaly, maternal age ≥15 years, maternal serum alpha-fetoprotein screen in gestational weeks 15-22, no pre-existing diagnoses of diabetes mellitus, and proficiency in English. Women with unexplained high alpha-fetoprotein levels (≥ 2 multiples of the median) were oversampled due to a particular interest in this biomarker for the original study aims.[16] Of the 3,038 women enrolled, 19 were lost to follow-up at birth leaving a cohort of 3,019 mother-child pairs. The POUCH study was approved from institutional review boards at

Michigan State University, Michigan Department of Community Health, and nine community hospitals.

A subcohort of women was selected for more detailed study to maximize resources when evaluating original study aims. The subcohort included all women who delivered preterm (<37 weeks), women who delivered at term but had unexplained high maternal serum alpha-fetoprotein levels, and a race-stratified sample of women with term deliveries and normal maternal serum alpha-fetoprotein levels (i.e., 72% African American and 23% White/other women in this category). Women enrolled in the POUCH study but not meeting these criteria comprised the "non-subcohort". Women in the subcohort were contacted periodically for different follow-up studies (2005-2006; 2006-2007), while the non-subcohort received minimal contact.

In fall of 2007, follow-up surveys on LTPA during pregnancy and child health outcomes were sent to all POUCH study participants who had not declined further contact after delivery and whose children were living with them (n=1629 non-subcohort; n=1261 subcohort). Women in the non-subcohort were sent a single mailing which asked them to complete and return an enclosed survey. No further contact was attempted for the non-subcohort. Women in the subcohort were sent the same mailing; however, phone contact was attempted to encourage participation, and follow-up mailings were sent.

For this investigation, women who delivered preterm < 37 weeks of gestation were excluded (non-subcohort n=0, subcohort n=335). A total of 1200 non-subcohort and 299 subcohort women failed to return the follow-up survey, and there was incomplete follow-up information on LTPA during pregnancy (non-subcohort n=11, subcohort n=31) or current child height and weight (non-subcohort n=0, subcohort n=4) among the

respondents. Thus the sample for this investigation included 418 (26% of eligible) non-subcohort and 592 (67% of eligible) subcohort women.

Study Protocol

The POUCH study has been described elsewhere in detail.[16] Briefly, participants met with a study nurse at enrollment to sign consent forms, completed an in-person interview and a self-administered survey, and had biological samples collected. The interview and self-administered survey provided information on maternal size, race/ethnicity, education, marital status, enrollment in Medicaid, and smoking at mid-pregnancy. Maternal pre-pregnancy body mass index (BMI, kg/m^2) was calculated from self-reported pre-pregnancy weight and height values.

Birth weight, child gender, maternal age at delivery, and parity were determined through chart review. Gestational age was calculated using the last menstrual period unless it disagreed by > 2 weeks with ultrasound conducted prior to 25 weeks gestation, in which case the ultrasound value was used. Sex and gestational-age specific birth weight z-scores were calculated as the observed minus the mean birth weight divided by the population standard deviation using birth weight standards from Kramer et al.[17] Offspring were classified as small-, appropriate, or large-for-gestational-age (SGA, AGA, or LGA) if their sex and gestational age-specific birth weights were $\leq 10^{th}$, between the 10^{th} and 90^{th}, or $\geq 90^{th}$ percentile, respectively.[18]

At follow-up, women reported their children's current age, height (in), weight (lbs), and leisure-time behavior. Reported height and weight values were used to calculate child BMI (kg/m^2). Age- and sex-specific BMI percentile values were calculated using the 2000 Centers for Disease Control and Prevention (CDC) growth

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charts.[19] Child BMI values that were biologically implausible according to CDC criteria (i.e., any BMI z-score value calculated as less than -4.0 or greater than +5.0 units) were excluded from further analyses (non-subcohort n=14; subcohort n=56).[19] Children were classified into weight status categories of "underweight" ($<5^{th}$ percentile), "healthy weight" (5^{th} -< 85^{th} percentile), "overweight" (85^{th} -< 95^{th} percentile), and "obese" ($\geq 95^{th}$ percentile). Women reported their child's choice of leisure-time behavior as "mostly sedentary", "some sedentary and some physically active", or "mostly physically active".[20]

Women also reported gestational weight gain and LTPA participation for the POUCH pregnancy, as well as current height and weight (used to calculate current maternal BMI) and LTPA at follow-up. Women were classified into weight gain categories (less than, within, and greater than recommended) based on the 1990 Institute of Medicine recommendations according to their pre-pregnancy BMI.[21] Women recalled whether they participated in any LTPA during their POUCH pregnancy. If so, they were asked to recall the type, average duration (min/d), and average frequency (d/wk) of up to two activities performed most often during a typical week while pregnant. To quantify intensity, metabolic equivalent (MET) values were assigned to each reported activity using the Compendium for Physical Activities.[22] Women who reported at least 150 min/wk of at least moderate intensity LTPA (i.e., ≥ 3 METs) were classified as "meeting/exceeding LTPA recommendations" according to the American College of Obstetricians and Gynecologists (ACOG) recommendation for LTPA during pregnancy.[23] Women reporting LTPA below this threshold were classified as "insufficiently active" while women reporting no LTPA were classified as "inactive".

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Women also reported their current (within the past month) LTPA levels and were classified in the same manner. Information on other domains of physical activity (i.e., occupational, household, etc) was not collected.

In order to consider simultaneously the effects of maternal LTPA during pregnancy and child leisure-time behavior on child weight status, a categorical "Maternal/Child LTPA" variable was created. First, two dichotomous variables were created to classify women as participating in any vs. no LTPA during pregnancy and children as having sedentary vs. non-sedentary (includes "some active and some sedentary" and "mostly active") leisure-time behavior. Participants were then classified as "any LTPA during pregnancy and non-sedentary child behavior" (+ / +), "any LTPA during pregnancy and sedentary child behavior" (+ / -), "inactivity during pregnancy and non-sedentary child behavior" (- / +), or "inactivity during pregnancy and sedentary child behavior" (- / -).

Statistical Analyses

Because of the sampling schemes employed to create the original POUCH study cohort and subcohort, and the differing follow-up strategies, primary analyses were conducted separately for non-subcohort and subcohort participants. All analyses were conducted using SAS version 9.1. Significance was set as a two-tailed Alpha level of $\leq$ 0.05.

Polytomous logistic regression analyses were used to assess the main effects of maternal LTPA during pregnancy (reference group = inactive) and child leisure-time behavior (reference group= sedentary) on child weight status (reference group = Healthy Weight). Separate polytomous logistic regression models then evaluated the association

between between maternal/child LTPA (reference group = + / +) and odds of child weight status. Stepwise regression methods were used to build adjusted models. The following variables were considered as covariates based on previous literature: maternal race (among the subcohort only), pre-pregnancy and current maternal BMI, gestational weight gain, maternal report of smoking during pregnancy, enrollment in Medicaid, relationship status, educational level, occupational status, child gender, and birth weight for gestational age group. Likelihood ratio tests were used for significance testing in building adjusted models. Any variable that altered parameter estimates more than 10% was examined as a potential confounder or mediator.

RESULTS

Within both the non-subcohort and subcohort, follow-up survey nonresponders included significantly more women who were African American, younger age, had less than high school education, were single, enrolled in Medicaid and smoked during pregnancy, compared to participating women (data not shown). Among participating women, maternal characteristics differed substantially between the non-subcohort and subcohort (Table 5.1). While some differences were expected due to the sampling strategy used to create the subcohort (i.e., 4.5% vs. 30.6% African American women in the non-subcohort vs. subcohort in this sample), other differences may reflect self-selection in relation to the intensity of follow-up efforts. The subcohort included more women who were younger, less educated, single, enrolled in Medicaid, had higher BMI values pre-pregnancy and currently, smoked during pregnancy, and were inactive during pregnancy and currently.

Some child characteristics also differed by subcohort status (Table 5.2). The non-subcohort included fewer children who were born SGA and more born LGA compared to the subcohort. Mean child BMI was 16.3 ± 2.4 kg/m^2 among the non-subcohort and 16.7 ± 2.8 kg/m^2 among the subcohort, corresponding to BMI z-score values of 0.27 ± 1.45 and 0.39 ± 1.57, respectively. Significantly more children in the subcohort were classified as obese (21.6%) compared to the non-subcohort (14.9%); however, the percent of children classified as underweight were equally represented in both the non-subcohort (10.6%) and subcohort (10.5%). Underweight children were excluded from further analyses due to the small number in this category and a primary interest in odds of overweight or obese status vs, healthy weight status.

Child leisure-time behavior was similar between the non-subcohort and subcohort; however, combined maternal/child LTPA was different between groups. The subcohort had a higher percentage of "inactivity during pregnancy and sedentary child behavior" (- / -) and a lower percentage of "any LTPA during pregnancy and non-sedentary child behavior" (+ / +) compared to the non-subcohort (Table 5.2).

Among the non-subcohort, being insufficiently active or meeting LTPA recommendations during pregnancy were each associated with ~50% reduced odds of child overweight and obese status (Table 5.3). These estimates were of borderline statistical significance, even after adjusting for child sedentary behavior and Medicaid enrollment. Being insufficiently active or meeting LTPA recommendations during pregnancy were also associated with non-significantly reduced odds of child obesity among the subcohort; however, LTPA during pregnancy significantly increased odds of child overweight status by about two-fold in this group.

Child leisure-time behavior was not significantly associated with child weight status in either group. Among the non-subcohort, being classified as "some sedentary/some active" or "mostly active" were associated with lower odds of child obesity, but non-significantly higher odds of child overweight. Within the subcohort, "some sedentary/some active" and ",mostly active" child behavior were related to lower odds of both child overweight and obese status, but these estimates were not significant in adjusted analyses.

Similar to the main effect results, associations among the combined maternal/child LTPA variable and child overweight status varied between non-subcohort and subcohort participants (Table 5.4). Among the non-subcohort, maternal inactivity during pregnancy combined with either child non-sedentary (-/+) or sedentary behavior (-/-) was associated with non-significant increased odds of child overweight status ($p > 0.05$). In contrast, among the subcohort, maternal inactivity during pregnancy combined with non-sedentary child behavior was associated with significantly lower odds of child overweight (aOR=0.49, 95%CI: 0.27-0.89). The association between maternal inactivity during pregnancy combined with child sedentary behavior and child overweight status among the subcohort approached unity and was non-significant.

Results for child obesity were more consistent among the non-subcohort and subcohort, with both groups displaying increased odds associated with maternal inactivity during pregnancy combined with either non-sedentary or sedentary child behavior (Table 5.4). In unadjusted analyses, odds of obesity were ~2.5-3.0 times higher when both the mother and child were classified as inactive/sedentary as compared to both being active/non-sedentary. Adjustment for maternal covariates attenuated results within both

the non-subcohort and subcohort to statistical non-significance, yet point estimates still indicated ~2.0-2.5 times the odds of child obesity when both the mother and child were classified as inactive/sedentary. Estimates for the effect of any maternal LTPA during pregnancy combined with child sedentary behavior (+/-) on child obesity were non-significant in both the non-subcohort and subcohort, but tended to be associated with increased odds among the non-subcohort.

Since associations for the main effects of LTPA during pregnancy and child leisure-time behavior as well as the interactive effect of maternal/child LTPA on odds of child obesity were similar for the non-subcohort and subcohort, we considered combining these groups in secondary analyses. Formal tests for interaction between subcohort status and LTPA during pregnancy or maternal/child LTPA on odds of child obesity was non-significant. Thus the non-subcohort and subcohort were combined to increase power and improve ability to consider covariates. Overweight children were excluded from these analyses due to the contrasting effects observed for the separate and combined effects of LTPA during pregnancy and child leisure-time behavior by subcohort status. Once children from the two groups were combined and overweight children were excluded, 25.0% (176/703) were classified as obese, with the remainder classified as healthy weight (reference group).

Unadjusted results from the combined analyses showed ~50% reduced odds of child obesity associated with LTPA during pregnancy or with some sedentary/some active child leisure-time behavior and ~2.0-3.0 times the odds of child obesity associated with maternal inactivity during pregnancy combined with either non-sedentary or sedentary child behavior (Unadjusted Models, Table 5.5). Adjustment for maternal

race/ethnicity, Medicaid enrollment, and pre-pregnancy BMI attenuated these relationships to borderline statistical significance (Models 1 and 2, Table 5.5). Maternal activity during pregnancy combined with sedentary child behavior was also associated with increased odds of obesity, however, the confidence intervals were wide and included unity in both unadjusted and adjusted models. Appropriateness of birth weight for gestational age category (i.e., SGA, AGA, or LGA) was subsequently added to Model 2 and examined as a possible mediator of the relationship between LTPA during pregnancy and child obesity. The addition of this variable was not significant and did not change parameter estimates appreciably, suggesting that birth weight did not mediate the effect of maternal/child LTPA on child obesity (data not shown). No other covariate significantly entered the main effects or interaction models.

Both separate (i.e., non-subcohort and subcohort) and combined analyses were repeated after removing women with unexplained high maternal serum alpha-fetoprotein levels, which is associated with increased risk of preterm delivery (n=0 non-subcohort, n=95 subcohort). The direction of relationships remained unchanged; however, parameter estimates for the effects of maternal/child LTPA on odds of child obesity became more extreme and remained statistically significant even when adjusted for maternal race/ethnicity, Medicaid enrollment, and pre-pregnancy BMI. Specifically, within combined adjusted analyses, increased odds of child obesity were observed for maternal inactivity during pregnancy combined with non-sedentary (aOR=1.52, 95% CI: 0.98-2.33) or with sedentary child behavior (aOR=2.20, 95% CI: 1.11-4.35).

DISCUSSION

Our purpose was to evaluate the separate and combined effects of maternal LTPA during pregnancy and child LTPA on child weight status at 3-9 years of age. We hypothesized that LTPA during pregnancy would be associated with reduced odds of child overweight and obesity and that odds of overweight and/or obesity would be highest when both the mother and child were classified as inactive/sedentary as compared to when both were active/non-sedentary. While results for child overweight status were mixed, being insufficiently active or meeting LTPA recommendations during pregnancy tended to reduce the odds of child obesity by 20-40% ($p>0.05$) within both the non-subcohort and the subcohort. Maternal inactivity during pregnancy combined with either child non-sedentary or sedentary behavior also tended to be associated with higher odds of child obesity in both groups. Although not statistically significant in adjusted models, odds of child obesity were highest when both the mother and child were classified as inactive/sedentary, whether evaluated separately within the non-subcohort and subcohort, or within the combined sample.

Combining the non-subcohort and subcohort allowed us to examine the separate and combined effects of maternal LTPA and child leisure-time behavior on odds of obesity within a diverse sample of women while also considering important covariates. Adjustment for maternal race/ethnicity, Medicaid enrollment, and pre-pregnancy BMI status attenuated our results to borderline statistical significance. However, practically speaking, they are still suggestive of a protective main effect for maternal LTPA during pregnancy and for a protective interactive effect of maternal LTPA during pregnancy combined with non-sedentary child behavior on childhood obesity risk. Other covariates

which have been associated previously with child obesity, including gestational weight gain, maternal educational level, smoking during pregnancy, current maternal BMI, and parity, did not significantly alter our results and were not included in the final model.

Past researchers have considered the effect of maternal or child LTPA participation on child weight status separately, but never combined as we have done. To our knowledge, James Clapp, MD conducted the only study to consider lasting effects of LTPA during pregnancy on child size.[11] He found that offspring of women who exercised throughout pregnancy (n=20) had lower body fatness measures at 5 years of age compared to offspring of women who had exercised pre-pregnancy but voluntarily stopped activity during pregnancy (n=20). This study was conducted using a small, select group of women and demonstrated that LTPA during pregnancy could affect child body size/composition in the absence of confounding factors such as maternal overweight. Unfortunately no information on child LTPA or diet behaviors was collected. Our results for the main effect of LTPA during pregnancy corroborate Clapp's findings. Although we did not have measures of body fatness, we found that participating in insufficient amounts of LTPA or meeting LTPA recommendations were associated with ~50% significantly reduced odds of child obesity within the non-subcohort and the subcohort. Adjustment for child leisure-time behavior and maternal characteristics attenuated these results to borderline statistical significance.

The mechanism for the effect of LTPA during pregnancy on child body size is unclear. Clapp found the offspring of the more active women were also lighter and leaner at birth compared to the control group.[11] Other studies have reported that LTPA before and/or during pregnancy is associated with lower odds of giving birth to an LGA

infant.[24, 25] Thus, it is possible that maternal LTPA alters fetal growth to reduce fat stores at birth and may modify metabolic mechanisms throughout childhood, leading to less excess fat storage. It is also possible that women who choose to engage in LTPA during pregnancy provide a more physically active environment for their children, thereby influencing child growth and weight status. Neither hypothesis has been tested. Regardless of the mechanism involved, our results support a role for LTPA during pregnancy to affect child weight status, even when controlling for children's current sedentary behavior. Additionally, birth size did not appear to mediate the relationship between maternalLTPA during pregnancy and child size in our study.

In contrast to the paucity of data on LTPA during pregnancy and child weight status, child LTPA and/or sedentary behavior has been studied extensively in relation to weight status. Most studies report negative correlations between LTPA and fatness among children, while relationships between LTPA and BMI weight categories tend to be null.[12-15, 26-29] Studies on sedentary behavior among children have consistently reported improved weight indices associated with fewer hrs/wk spent in sedentary activity.[30] It is possible that sedentary behavior increases risk of child overweight/obesity through displacing LTPA, increasing energy intake via snacking, effects of food advertising on TV, and/or decreased metabolic rate during sedentary time.[30] Our results showed that children choosing some sedentary/some active or mostly active leisure-time behaviors had non-significantly reduced odds of child obesity within both the non-subcohort and the subcohort. Sedentary children with mothers who were active during pregnancy had increased odds of obesity in combined analyses; however these estimates had wide confidence intervals that included unity (Table 5.4). Children who were sedentary and

also had mothers who were inactive during pregnancy had almost three times the odds of obesity in combined, unadjusted analyses. While adjustment for maternal factors attenuated this relationship, maternal inactivity combined with sedentary child activity still showed borderline significance indicating almost twice the odds of obesity.

Unlike odds of obesity, results for the relationships between maternal LTPA during pregnancy or maternal/child PA and odds of child overweight status were quite different between the non-subcohort and subcohort. It is unclear why LTPA during pregnancy would be associated with increased odds of child overweight while maternal inactivity during pregnancy combined with non-sedentary child activity would be associated with significantly decreased odds of overweight within the subcohort. One possibility is that the overweight category included a greater number of children who were misclassified by maternal reports of their height and weight than did the obese category, resulting in variable associations. Past literature suggests that parentally-reported height and weight values correctly classify obese children more often than overweight children.[31-33] Thus, the results seen for odds of obesity may be more consistent between the non-subcohort and subcohort due to the more accurate maternal identification of obese children.

This study is limited by the reliance on maternally reported values for child height, weight and leisure-time behavior, as well as the women's recalled information for LTPA during pregnancy. Previous evidence on the validity of maternal report of child body size indicates moderate to good agreement for individual measures of height or weight, but poorer agreement for weight classification by BMI (kappa=0.34 for girls and 0.41 for boys).[33-35] We excluded data from children with BMI values flagged as

biologically implausible by the CDC criteria to help improve the validity of our outcome variable. We used a proxy measure of child leisure-time behavior, asking mothers to characterize their children as mostly sedentary, some sedentary/some active, or mostly active in their leisure-time. It would have been more ideal to have direct, objective measures of child LTPA. However, LTPA intervention studies have not been able to demonstrate measureable improvements in child weight status, while interventions to reduce sedentary behavior have more consistently shown reductions in overweight status.[30, 36, 37] It is possible that time spent in sedentary behavior is easier for parents/children to report, thus greater effects on weight status are able to be demonstrated in relation to sedentary behavior. We also lacked information on children's dietary patterns which may have affected their weight status.

Finally, information on LTPA during pregnancy was recalled retrospectively at 3-9 years postpartum, thus recall bias cannot be discounted. Bias due to recall error in our study may have been reduced by using a categorical variable to indicate any vs. no LTPA during pregnancy. Differential bias due to either maternal report of child body size or recall error is less likely because women were not told of the study aims and responded to these questions as part of a larger questionnaire on maternal and child behaviors.

Despite these limitations, our results add significantly to the existing literature on risk factors for child obesity. While past research provides evidence for the role of both maternal and child LTPA participation on child body size, no previous study has considered the simultaneous effect of these two factors as we have done. Insufficient activity and/or meeting LTPA recommendations during pregnancy were each associated with ~30-50% reduced odds of child obesity in the non-subcohort and the subcohort.

These effects were borderline significant even after controlling for child sedentary behavior and maternal covariates. Furthermore, although statistically non-significant in adjusted analyses, odds of obesity were highest when both the mother and child were classified as inactive/sedentary compared to active/non-sedentary.

Future work should further explore the inter-relationships among maternal and child LTPA and child weight status, and seek to determine plausible mechanisms through which maternal LTPA during pregnancy may affect child body size. Prospective, trimester-specific measures of LTPA during pregnancy combined with more objective measures of child LTPA levels are needed to test and refine our results. Beneficial maternal health effects of LTPA are already recognized.[38] Our results suggest further that engaging in LTPA during pregnancy may improve offspring health by decreasing the odds of obesity. Overall, our results indicate that both maternal LTPA during pregnancy and child leisure-time behavior are important factors in the development of child obesity.

Table 5.1: Maternal characteristics of the POUCH study non-subcohort and subcohort*

	Non-Subcohort N (%)	Subcohort N (%)	Chi-Square p-value
N	404	536	
Maternal Race			
White/Other	386 (95.5)	372 (69.4)	<0.001
African American	18 (4.5)	164 (30.6)	
Maternal Age at Delivery			
<20 yrs	21 (5.2)	50 (9.3)	
20-<30 yrs	194 (48.0)	306 (57.1)	<0.001
≥ 30 yrs	189 (46.8)	180 (33.6)	
Maternal Education			
< High School	28 (6.9)	70 (13.1)	
High School	73 (18.1)	134 (25.0)	<0.001
> High School	303 (75.0)	332 (61.9)	
Medicaid			
Yes	94 (23.3)	231 (43.1)	<0.001
Relationship Status			
Single	47 (11.6)	146 (27.2)	<0.001
Smoking during Pregnancy			
At least some	28 (6.9)	80 (14.9)	<0.001
Pre-pregnancy Maternal BMI			
< 25 kg/m^2	221 (54.7)	265 (49.4)	
25-<30 kg/m^2	111 (27.5)	118 (22.0)	<0.001
≥ 30 kg/m^2	72 (17.8)	153 (28.5)	
Weight Gain During Pregnancy			
Low	45 (11.3)	87 (16.7)	
Recommended	143 (35.9)	169 (32.5)	0.062
High	210 (52.8)	264 (50.8)	
Maternal BMI at Follow-Up			
< 25 kg/m^2	190 (47.0)	187 (34.9)	
25-<30 kg/m^2	105 (26.0)	146 (27.2)	<0.001
≥ 30 kg/m^2	109 (26.7)	203 (37.9)	
LTPA During Pregnancy[$]			
Inactive	161 (39.8)	258 (48.1)	
Insufficiently Active	121 (29.9)	124 (23.1)	0.020
Meeting Recommendations	122 (30.2)	154 (28.7)	
LTPA at Follow-Up[$]			
Inactive	100 (24.7)	178 (33.2)	
Insufficiently Active	100 (24.7)	107 (19.9)	0.014
Meeting Recommendations	204 (50.5)	251 (46.8)	

*Includes only POUCH study participants who gave birth at term and were enrolled in the 2007 follow-up study

[$]LTPA= leisure-time physical activity

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Table 5.2: Child characteristics of the POUCH study non-subcohort and subcohort*

	Non-Subcohort N (%)	Subcohort N (%)	Chi-Square p-value
N	404	536	
Child Gender			
Male	194 (48.0)	259 (48.3)	0.927
Size at birth			
AGA	313 (77.5)	416 (77.6)	
SGA (≤ 10th %tile)	18 (4.5)	57 (10.6)	<0.001
LGA (≥ 90th %tile)	73 (18.1)	63 (11.8)	
Parity			
Nulliparous	179 (44.3)	219 (40.9)	0.289
Child Age at Follow-Up			
< 4 years	75 (18.6)	74 (13.8)	
4-<6 years	177 (43.8)	266 (49.6)	0.082
≥ 6 years	152 (37.6)	196 (36.6)	
Child BMI at Follow-Up			
Underweight (<5th %tile)	43 (10.6)	56 (10.5)	
Healthy Weight (5th -< 85th %tile)	244 (60.4)	283 (52.8)	0.042
Overweight (85th -< 95th %tile)	57 (14.1)	81 (15.1)	
Obese (≥ 95th %tile)	60 (14.9)	116 (21.6)	
Child Leisure-Time Behavior			
Mostly Sedentary	47 (11.6)	83 (15.5)	
Some Sedentary/ Some Active	181 (44.8)	209 (39.0)	0.103
Mostly Active	176 (43.6)	244 (45.5)	
Maternal/Child LTPA ψ			
+ / +	219 (54.2)	247 (46.1)	
+ / -	24 (5.9)	31 (5.8)	0.031
- / +	138 (34.2)	206 (38.4)	
- / -	23 (5.7)	52 (9.7)	

* Includes only POUCH study participants who gave birth at term and were enrolled in the 2007 follow-up study

$ LTPA= leisure-time physical activity

ψ Maternal/Child LTPA "+ / +" represents any maternal LTPA during pregnancy and child non-sedentary activity; "+ / -" is any maternal LTPA during pregnancy and child sedentary activity; "- / +" is maternal inactivity during pregnancy and child non-sedentary activity; "- / -" is maternal inactivity during pregnancy and child sedentary activity

Table 5.3: Associations among maternal LTPA during pregnancy, child leisure-time behavior, and child weight status at 3-9 years (Reference: Healthy Weight) within the POUCH study non-subcohort and subcohort

	Overweight		Obese	
	Univariate OR[†] (95% CI)	**Adjusted OR[‡] (95% CI)**	**Univariate OR[†] (95% CI)**	**Adjusted OR[‡] (95% CI)**
Non-Subcohort (n=361)[§]				
LTPA during Pregnancy (ref: Inactive)[ψ]				
Insufficiently Active	0.53 (0.29, 1.07)	0.52 (0.25, 1.07)	0.47* (0.24, 0.96)	0.59 (0.28, 1.22)
Meeting LTPA Recs	0.54 (0.27, 1.09)	0.52 (0.26, 1.06)	0.49* (0.24, 0.99)	0.52 (0.26, 1.06)
Child Behavior (ref: Mostly Sedentary)				
Some Sedentary/ Some Active	1.27 (0.45, 3.59)	1.34 (0.47, 3.84)	0.44 (0.19, 1.03)	0.53 (0.22, 1.27)
Mostly Active	1.44 (0.51, 4.10)	1.54 (0.54, 4.41)	0.73 (0.33, 1.64)	0.82 (0.36, 1.90)
Subcohort (n=480)[§]				
LTPA during Pregnancy (ref: Inactive)[ψ]				
Insufficiently Active	1.69 (0.90, 3.17)	1.97* (1.03, 3.78)	0.55* (0.30, 1.00)	0.73 (0.39, 1.36)
Meeting LTPA Recs	1.72 (0.96, 3.07)	2.15* (1.17, 3.94)	0.57* (0.34, 0.97)	0.80 (0.46, 1.42)
Child Behavior (ref: Mostly Sedentary)				
Some Sedentary/ Some Active	0.64 (0.32, 1.29)	0.61 (0.30, 1.27)	0.51 * (0.27, 0.97)	0.70 (0.35, 1.40)
Mostly Active	0.66 (0.33, 1.32)	0.54 (0.26, 1.11)	0.86 (0.47, 1.58)	0.80 (0.42, 1.53)

[§] excludes underweight children (n=43 non-subcohort, n=56 subcohort)

[†] Univariate OR's are unadjusted for any other variable

[‡] Adjusted OR's are mutually adjusted for variables shown in table as well as Medicaid enrollment for the Non-subcohort and maternal race (White/Other vs. African American), pre-pregnancy BMI, and Medicaid enrollment for the Subcohort.

[ψ] LTPA during pregnancy: "Inactive" includes women reporting no LTPA during pregnancy, "Insufficiently Active" includes women reporting less than recommended amounts of LTPA during pregnancy (<150 min/wk of moderate LTPA), "Meeting LTPA Recs" includes women reporting ≥150 min/wk of at least moderate LTPA during pregnancy

* $p<0.05$

Table 5.4: Associations among maternal/child LTPA and child weight status at 3-9 years (Reference: Healthy Weight) within the POUCH study non-subcohort and subcohort

	Overweight		Obese	
	OR (95% CI)	**aOR (95% CI)[†]**	**OR (95% CI)**	**aOR (95% CI)[†]**
Non-Subcohort (n=361)[§]				
Maternal / Child LTPA (Ref: + / +)[ψ]				
+ / -	0.32 (0.04, 2.54)	0.33 (0.04, 2.55)	1.89 (0.63, 5.63)	1.72 (0.57, 5.63)
- / +	1.75 (0.95, 3.24)	1.76 (0.94, 3.28)	2.13* (1.14, 4.00)	1.86 (0.98, 3.54)
- / -	1.73 (0.52, 5.74)	1.74 (0.52, 5.84)	3.02* (1.04, 8.82)	2.47 (0.83, 7.39)
Subcohort (n=480)[§]				
Maternal / Child LTPA (Ref: + / +)[ψ]				
+ / -	1.70 (0.67, 4.33)	1.75 (0.68, 4.51)	0.96 (0.30, 3.08)	1.06 (0.32, 3.55)
- / +	0.53* (0.31, 1.00)	0.49* (0.27, 0.89)	1.64* (1.01, 2.64)	1.25 (0.75, 2.01)
- / -	0.95 (0.40, 2.27)	0.83 (0.35, 2.01)	2.42* (1.20, 4.89)	1.76 (0.84, 3.71)

[§] excludes underweight children (n=43 non-subcohort, n=56 subcohort)

[†] Non-subcohort model is adjusted for Medicaid. Subcohort model is adjusted for maternal race (White/Other vs. African American), Medicaid enrollment, and pre-pregnancy BMI (<25, ≥25 kg/m^2)

[ψ] Maternal/Child LTPA "+ / +" represents any maternal LTPA during pregnancy and child non-sedentary activity; "+ / -" is any maternal LTPA during pregnancy and child sedentary activity; "- / +" is maternal inactivity during pregnancy and child non-sedentary activity; "- / -" is maternal inactivity during pregnancy and child sedentary activity.

* $p<0.05$

Table 5.5: The effects of LTPA during pregnancy and child leisure-time behavior on odds of obesity among children 3-9 years in the POUCH cohort (n=703[§]).

	Obesity (n=176) (Ref: Healthy Weight)		
Main Effects Models			
	Unadjusted OR (95% CI)	**Model 1[†] aOR (95% CI)**	**Model 2[†] aOR (95% CI)**
LTPA during Pregnancy (ref: Inactive)[$]			
Insufficiently Active	0.48* (0.31, 0.76)	0.51* (0.32, 0.80)	0.68 (0.42, 1.09)
Meeting LTPA Recs	0.52* (0.34, 0.78)	0.53* (0.35, 0.81)	0.74 (0.47, 1.15)
Child Behavior (ref: Mostly Sedentary)			
Some Sedentary/ Some Active	0.47* (0.28, 0.78)	0.53* (0.31, 0.88)	0.67 (0.39, 1.17)
Mostly Active	0.80 (0.49, 1.30)	0.88 (0.54, 1.44)	0.84 (0.50, 1.42)
Interaction Models			
Maternal / Child LTPA (Ref: + / +)[Ψ]	**Unadjusted OR (95% CI)**	**Model 1[‡] aOR (95% CI)**	**Model 2[‡] aOR (95% CI)**
+ / -	1.31 (0.59, 2.91)	1.34 (0.59, 3.04)	1.40 (0.61, 3.20)
- / +	1.91* (1.30, 2.78)	1.50* (1.01, 2.24)	1.42 (0.95, 2.12)
- / -	2.84* (1.59, 5.09)	1.94* (1.05, 3.60)	1.78 (0.95, 3.34)

[§] Excludes underweight (n=119) and overweight (n=138) children

[†] Main Effects Model 1 is mutually adjusted for both main effects variable. Model 2 is adjusted for further adjusted for for maternal race (White/Other, African American), Medicaid enrollment, and pre-pregnancy BMI (<25, ≥25 kg/m^2).

[‡] Interaction Model 1 is adjusted for maternal race (White/Other, African American) and Medicaid enrollment. Model 2 is adjusted for covariates in Model 1 + pre-pregnancy BMI (<25, ≥25 kg/m^2).

[$] LTPA during pregnancy: "Inactive" includes women reporting no LTPA during pregnancy, "Insufficiently Active" includes women reporting less than recommended amounts of LTPA during pregnancy (<150 min/wk of moderate LTPA), "Meeting LTPA Recs" includes women reporting ≥150 min/wk of at least moderate LTPA.

[Ψ] Maternal / Child LTPA"+ / +" represents any maternal LTPA during pregnancy and child non-sedentary activity; "+ / -" is any maternal LTPA during pregnancy and child sedentary activity; "- / +" is maternal inactivity during pregnancy and child non-sedentary activity; "- / -" is maternal inactivity during pregnancy and child sedentary activity.

* $p<0.05$

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CHAPTER SIX

RELIABILITY OF RECALLING LEISURE-TIME PHYSICAL ACTIVITY PERFORMED DURING PREGNANCY

ABSTRACT

Our purpose was to evaluate the reliability of recalling leisure-time physical activity (LTPA) performed during pregnancy among postpartum women. **Methods:** Women (n=311) reported min/wk spent in moderate and vigorous LTPA at their first prenatal care visit. Total min/wk of LTPA was calculated. At 15-30 months postpartum, 82 women recalled the type, duration, and frequency of LTPA during the trimester of their original interview. Recalled min/wk of moderate, vigorous, and total LTPA were calculated. **Results:** Mean differences in observed-recalled LTPA were small but standard deviations were large (-6.0 ± 175.7, 3.6 ± 71.5, and -2.4 ± 193.6 min/wk for moderate, vigorous, and total LTPA, respectively). Recalled vigorous (r_s=0.34, p=0.002) and total (r_s=0.28, p=0.016) LTPA values were significantly correlated with original reports, but this was not true for moderate LTPA (r_s=0.10, p=0.350). Older age, higher income, having a healthy weight, and participating in recommended amounts of LTPA at follow-up were associated with better total LTPA recall ability. There was high percent agreement for original vs. recalled report of any moderate, vigorous, or total LTPA (70-79%), but kappa values were low (0.015-0.183). **Conclusions:** Correlations between original and recalled LTPA are low to moderate, percent agreement for participation in LTPA during pregnancy is high, but kappa values are low. Participant characteristics may influence reliability of LTPA recall.

INTRODUCTION

Leisure-time physical activity (LTPA) during pregnancy has been associated with a wide range of health benefits, including decreased risk of gestational diabetes, preeclampsia, and maternal obesity.[1-3] Thus, the American College of Obstetrics and Gynecology (ACOG) recommended in 2002 that all pregnant women participate in at least 30 minutes of moderate LTPA on most days of the week.[4] More recently in 2008, the U.S. Government released evidenced-based LTPA guidelines for Americans which also stated that previously sedentary pregnant women should engage in at least 150 minutes of moderate LTPA per week, while habitual exercisers may continue more vigorous activities under the supervision of their health care providers.[5] While past research has focused on the effects of LTPA during pregnancy on birth outcomes, investigators are beginning to evaluate possible relationships with later maternal/child health outcomes.

Several questionnaires have been validated for measuring multiple domains of physical activity, including LTPA, among women who are currently pregnant;[6, 7] however, prospective measurements of LTPA are often difficult to obtain. To facilitate epidemiological research on short- and long-term outcomes associated with LTPA during pregnancy, it is important to examine the reliability of historical recall of LTPA among postpartum women.

The Modifiable Activity Questionnaire (MAQ) was originally validated for historical recall of LTPA among Pima Indians; however, it was created specifically to be easily adapted to other populations and varying lengths of recall.[8, 9] Bauer et al. recently used the MAQ to assess the validity of recalled LTPA during pregnancy among women

six years postpartum.[10] Moderate to high agreement was found for recalled LTPA with that originally recorded at 20 and 32 weeks gestation, and 12 weeks postpartum.[10] Participants in the Bauer et al. study were Caucasian, relatively lean at follow-up, and many had participated in high amounts of LTPA during pregnancy. It is not known whether LTPA can be recalled reliably by women with more diverse socioeconomic status and LTPA patterns.

The purpose of this study was to evaluate the reliability of recalled LTPA during pregnancy compared to amounts reported at the first prenatal care visit among women who were 15-30 months postpartum. Additionally, we sought to determine whether participant characteristics influenced the reliability of the women's recall.

METHODS

Participants

Women were originally recruited from the waiting rooms of nine prenatal care clinics in Kent County, MI and asked to participate in a 15-20 minute face-to-face interview as part of the Michigan Alliance for the National Children's Study (MANCS) pilot study.[11, 12]Eligible women were currently pregnant, at their first prenatal care visit, 18-50 years old, and proficient in English or Spanish. From April-October 2006, 311 of 342 (91%) eligible women completed the interview. Of these, 299 provided complete LTPA information at the time of enrollment and agreed to be contacted for future studies.

From July 2008 - February 2009 women were contacted via mail and telephone and asked to complete a follow-up survey on pregnancy behaviors, birth outcomes and their toddler's health. One-hundred-ten women (37%) could not be located, despite paid internet searches. Of the remaining 188 women, 23 refused participation, 3 had

miscarried during their 2006 pregnancies, and 44 never responded to phone calls or mailings, leaving 118 who agreed to participate. Of these, 82 (28% of original cohort) provided complete LTPA recall information.

The original study was approved by the Institutional Review Boards of Michigan State University and the three hospitals with labor and delivery services in Kent County, MI – Spectrum Health, Metro Health, and St. Mary's Health Care Center. The Biomedical Institutional Review Board at Michigan State University approved the follow-up study. Women completed informed consent at the original recruitment and again for participation in the follow-up survey.

Original Data Collection

The original interview consisted of demographic questions, maternal LTPA participation and safety perceptions, and attitudes toward participating in hypothetical research procedures.[11, 12] Questions on LTPA were adapted from the 2001 Behavioral Risk Factor Survey.[13] Specifically, women reported whether or not they had participated in any moderate of vigorous physical activities during their free time in the past month (yes/no). If so, average durations (min/d) and frequencies (d/wk) were reported for a typical week. Interviewers described moderate activities as those causing light sweating or slight to moderate increases in breathing or heart rate, and vigorous activities as those that cause heavy sweating or large increases in breathing or heart rate. Scripted examples of moderate (e.g., brisk walking, gardening) and vigorous activities (e.g., running, aerobics) were given; however, specific activities were not recorded.

Minutes per week spent in moderate and vigorous LTPA were calculated. Total LTPA was recorded as the sum of moderate and vigorous LTPA. Women were

categorized as reporting any vs. no participation in moderate, vigorous, or total LTPA. Additionally, women reporting at least 150 minutes per week of total LTPA were classified as meeting ACOG recommendations.[4] Women also indicated whether or not they intended to be active throughout the remainder of their pregnancies as "yes", "no", or "it depends". Maternal age, educational level, race/ethnicity, relationship status, family income level, and parity were recorded. Finally, women reported their current gestational week of pregnancy or the trimester if they were unsure about the week.

Follow-up Data Collection

Women had the choice of completing the follow-up survey through the mail or over the internet. The MAQ was used to assess past and current LTPA. Participants recalled their LTPA for a typical week during five time-periods: the month before they knew they were pregnant, the first, second, and third trimesters, and the previous month. The time-period of recalled LTPA was matched to the trimester in which the woman completed the original interview. Women specified the type, duration (average min/d), and frequency (average d/wk) of up to five activities for each time-point. A standard list of 40 activities was provided for women to choose from, and they could write in other activities not on the list. To designate intensity, metabolic equivalent (MET) values were assigned to each reported activity using the compendium for physical activities.[14]

Minutes per week spent in each reported activity were calculated. To maintain comparability with previously collected data, amount of time (min/wk) recalled for moderate activity was calculated as the sum of all activities with a MET value of 3.0 to 5.9, while min/wk recalled for vigorous activity was calculated as the sum of all activities with a MET value $\geq$ 6.0. Total recalled min/wk of LTPA excluded any light intensity

activities (i.e., < 3.0 METs). Women were classified as recalling participation in any vs. no moderate, vigorous, or total LTPA. Women recalling participation in at least 150 min/wk of total LTPA were classified as meeting ACOG recommendations.[4] During follow-up, women also self-reported pre-pregnancy weight and height, gestational weight gain, and current weight. Both pre-pregnancy and current body mass index (BMI) values were calculated (kg/m^2).

Statistical Analyses

Chi-square analyses compared descriptive characteristics between women who did and did not participate in the follow-up study. Descriptive statistics were calculated for originally reported and recalled min/wk of moderate, vigorous, and total LTPA and mean differences were assessed. Physical activity data were non-normally distributed, thus Spearman rank-order correlation coefficients were used to assess relationships between originally reported and recalled min/wk of moderate, vigorous, and total LTPA for the sample as a whole and by subgroups of participant characteristics. The standard error of measurement was also calculated for recalled min/wk of moderate, vigorous, and total LTPA. Categorical agreement among originally reported and recalled LTPA (any vs. none and meeting vs. not meeting recommendations) was evaluated using percent agreement and Cohen's kappa, which corrects for chance agreement. All analyses were performed using SAS version 9.1 and significance was set at a two-tailed Alpha level of $p<0.05$.

RESULTS

Women who participated in the follow-up were significantly more likely to be older, more educated, of Non-Hispanic White race/ethnicity, married, have a higher

income, and to have completed their original interview in the 1st trimester (Table 6.1). According to the original report, participation in vigorous and total LTPA was more frequent among those who completed the follow-up; however, participation in moderate LTPA, likelihood of meeting ACOG guidelines, and intention to be active throughout pregnancy were not significantly different between those who did and did not complete the follow-up (Table 6.1).

Among women who completed the follow-up survey, average pre-pregnancy BMI was 23.7 ± 4.9 kg/m^2, reported gestational weight gain was 35 ±13 lbs, and BMI at follow-up was 25.1 ± 6.0 kg/m^2. Mean values of originally reported and recalled LTPA are shown in Table 6.2. Recalled LTPA for a typical week in the first trimester was used for all but six women whose first prenatal care visit fell in the second (n=5) or third (n=1) trimesters. Mean differences between originally reported and recalled LTPA values were small (-6.0 to 3.6 min/wk); however, wide ranges in recall ability were present. Values for the standard error of measurement for moderate (123 min/wk), vigorous (51 min/wk), and total (138 min/wk) LTPA indicate that women were more reliable at recalling vigorous than moderate or total LTPA.

Spearman correlations between originally reported and recalled moderate LTPA were not statistically significant for the group as a whole (r_s=0.10), or within any of the participant characteristic subgroups (Table 6.3). However, significant relationships were observed between original and recalled reports of vigorous (r_s=0.34) and total LTPA (r_s=0.28). Older women, those with higher income, and those with a BMI in the healthy range also had significant, moderately strong correlations between originally reported and recalled vigorous and total LTPA (r_s=0.36-0.56). Additionally, nulliparous women

displayed a significant correlation for original and recalled report of vigorous LTPA while parous women did not. Interestingly, women classified as meeting LTPA recommendations according to their current activity levels at follow-up showed a significant correlation between original and recalled total LTPA, while women classified as not meeting LTPA recommendations had a significant correlation for vigorous activity (Table 6.3). We were unable to evaluate differences in recall ability by education, race/ethnicity, and relationship status due to the homogeneity of our participants regarding these characteristics.

Percent agreement for women reporting any vs. no participation in moderate, vigorous, and total LTPA was high (74-79%, Table 6.4). However, using standard interpretation of the kappa statistic (i.e. kappa <0.2= poor, 0.2-0.39= fair, 0.4-0.59=moderate, 0.6-0.79=good, 0.8+= strong agreement)[15], results indicated poor agreement between original and recalled report of participation in LTPA during pregnancy. When categorizing women on meeting ACOG LTPA recommendations, there was moderate (57%) agreement between original and recalled reports, but the kappa value was 0.117 indicating poor agreement. Cell sizes were too small to determine whether categorical LTPA agreement varied by participant characteristics.

DISCUSSION

Our purposes were to evaluate the reliability of recalling LTPA during pregnancy among women 15-30 months postpartum, and to determine whether participant characteristics influenced reliability of recall. Our results indicate that recall of moderate LTPA was poor, but recalled amounts of vigorous and total LTPA were moderately correlated with original values. Maternal age, parity, income, maternal body size at time

of recall, and participation in recommended amounts of LTPA at time of recall each appeared to influence the reliability of recall on a continuous scale. When considered categorically, percent agreement for any vs. no participation in LTPA was high and percent agreement for meeting vs. not meeting ACOG recommendations was moderate; however kappa values were quite low.

Recalled amounts of moderate activity were non-significantly correlated with original values (r_s=0.10), whereas moderate and significant correlations were found for recalled vigorous (r_s= 0.34) and total LTPA (r_s=0.28). Similar correlations have been demonstrated for middle-aged women recalling LTPA occurring 1-5 years previously.[16, 17] Using a slightly different form of the MAQ than that used here, Chasan-Tabor et al. found poor one-year recall ability for moderate activity (r=0.15) and stronger recall ability for vigorous (r=0.52) and total (r=0.26) LTPA among a group of 131 women aged 39-65 yrs.[16] Similar correlations were demonstrated among 78 middle-aged women for the 3-5 year recall of moderate (r=0.16), vigorous (r=0.26), and total (r=0.20) physical activities.[17] Other studies involving mixed gender samples and/or longer recall lengths (10 to 30 yrs) have reported similar results for their female sub-cohorts as well, with correlations ranging from 0.25-0.47 for recall of moderate, 0.36-0.41 for vigorous, and 0.29-0.57 for total LTPA.[18-20] Thus, our results are in line with those reported previously for recalling LTPA and it appears that vigorous activities are more easily recalled than moderate intensity activities.

The one previous study to examine historical recall of LTPA performed during pregnancy found that values recalled six years postpartum were strongly correlated with originally measured LTPA at 20 and 32 weeks of gestation (r = 0.57 and 0.85,

respectively).[10] There are several reasons why our results are not as strong as those found by Bauer et al. Participants in the Bauer et al. study had much higher LTPA levels than our sample, which may have been more easily recalled. They had also been monitored carefully during pregnancy to record LTPA data via heart rate telemetry, accelerometry, and LTPA diaries.[10, 21, 22] Thus, it is possible that their apparent ability to recall LTPA was influenced by greater attention to their activity during pregnancy. Regardless, although our findings are not as strong, they do corroborate those of Bauer et al. using a larger and more diverse sample.

We found that correlations between originally reported and recalled LTPA were stronger for both vigorous and total LTPA among women ≥ 30 years old, those earning ≥ $50,000, and those with a healthy BMI (< 25 kg/m^2). Nulliparous women also displayed a stronger correlation for recall of vigorous LTPA, compared to parous women. While women meeting LTPA recommendations at the time of recall displayed a stronger correlation for total LTPA, women not meeting recommendations had a stronger correlation for recalling vigorous activity. Falkner et al. assessed the influence of participant characteristics on the recall of LTPA >30 years in the past.[23] The authors found that "underestimators" were younger while "overestimators" had higher levels of current LTPA compared to "good recallers".[23] All other participant characteristics (gender, education, marital status, BMI, pulse rate, and blood pressure) were unrelated to recall ability in their sample. Other investigators have reported that adjustment for age, length of recall interval, or current BMI did not significantly alter correlations between recalled and originally reported activity values; however, previous studies have not calculated stratum-specific correlation coefficients as we have done.[18, 24] It is possible

that recall of pregnancy-related LTPA is more susceptible to maternal characteristic influences, but more work is needed to confirm our findings.

Finally, our categorical analyses showed high percent agreement between original and recalled reports of participation in any moderate, vigorous, or total LTPA (70-79%), while percent agreement for meeting ACOG LTPA recommendations was moderate (57%). Unfortunately, kappa values were quite low for these comparisons and indicated poor agreement after controlling for chance. The condition of having high percent agreement and low kappa scores has been termed the "prevalence paradox".[25] When the prevalence of the outcome is very high or very low, agreement expected by chance increases and the magnitude of kappa decreases. In this situation, the interpretation of kappa is more ambiguous than standard guidelines, and it is recommended that both percent agreement and kappa scores be taken into consideration.[26] In our data 95% of women reported at least some moderate or vigorous LTPA at original data collection, thus it is not surprising that kappa values were low. Most previous studies on reliability of LTPA recall have not reported categorical agreement; however, one study on 10 year LTPA recall ability showed 70% agreement for reporting low vs. high amounts of vigorous LTPA and 66% agreement for total LTPA among 322 women.[18] Thus, our results are in line with those found previously among non-pregnant samples.

Some limitations of the present study must be noted. First, validation of originally reported LTPA levels was not conducted, so the possibility of bias and/or error in the original values cannot be discounted. However, the LTPA questions used in the original interview have been shown to be moderately to highly reliable for moderate (kappa 0.35-0.53) and vigorous (kappa 0.80-0.86) activities among U.S. adults, and moderately valid

for identifying recommended amounts of LTPA when compared to daily LTPA logs (kappa = 0.40-0.52).[13] Thus, we are fairly confident in our original report of LTPA. Additionally, a different survey of reporting LTPA was used at follow-up, thus some discrepancies between original and recalled amounts of LTPA may be due to survey differences.

Women participating in the follow-up study were substantially different from those who did not (Table 6.1), which limits the generalizability of our results. While original report of vigorous and total LTPA was more frequent among those who participated in follow-up, report of moderate LTPA, the likelihood of meeting ACOG LTPA recommendations, and intention to be/not be active throughout pregnancy did not significantly differ between those who did and did not participate in the follow-up. Finally, while small mean differences between recalled and originally reported amounts of LTPA were noted, individual differences were wide. Thus, some women grossly overestimated and others underestimated their original activities.

Despite limitations, our results corroborate previous reports on the reliability of historical recall of LTPA.[10, 16-20, 27] We found moderate reliability for recalling vigorous and total LTPA during pregnancy among women 15-30 months postpartum using rank-order spearman correlations. Older age, nulliparity, higher family income, and having a healthy BMI and participating in recommended amounts of LTPA at the time of recall were each associated with improved total LTPA recall ability. While kappa values for categorical analyses were low, percent agreement was high for recalling participation in moderate, vigorous and total LTPA and moderate for identifying women with recommended amounts of LTPA during pregnancy. Based on the results reported here

and those found by Bauer et al., we believe that future studies on the long-term outcomes associated with LTPA during pregnancy can consider use of historical recall of LTPA when prospective measurement is impractical.[10] Future research is needed to establish the reliability of historically recalling other domains of physical activity during pregnancy, such as occupational and household-related physical activity.

Table 6.1: Participant characteristics during pregnancy according to information reported during the original interview.

	Original Study N (%)	Did Not Complete Follow-Up N (%)	Completed Follow-Up N (%)	Chi-Square p-value*
N	299	217	82	
Age				
18-29 yrs	208 (69.6)	164 (75.6)	44 (53.7)	
30+ yrs	91 (30.4)	53 (24.4)	38 (46.3)	<0.001
Education				
< High School	68 (22.7)	65 (30.0)	3 (3.7)	<0.001
Race/ethnicity				
Non-Hispanic White	172 (57.5)	106 (48.9)	66 (80.5)	
Non-Hispanic Black	48 (16.1)	43 (19.8)	5 (6.1)	<0.001
Hispanic/Other	79 (26.4)	68 (31.3)	11 (13.4)	
Relationship Status				
Single	66 (22.2)	59 (27.4)	7 (8.5)	<0.001
Family Income[$]				
< $25,000	129 (43.9)	114 (53.8)	15 (18.3)	
$25 – 50,000	69 (23.5)	47 (22.2)	22 (26.8)	<0.001
> $50,000	96 (32.7)	51 (24.1)	45 (54.9)	
Parity				
Nulliparous	124 (41.5)	84 (38.7)	40 (48.8)	0.115
Trimester of Interview				
1st	248 (82.9)	172 (79.3)	76 (92.7)	
2nd	42 (14.1)	37 (17.1)	5 (6.1)	0.023
3rd	9 (3.0)	8 (3.7)	1 (1.2)	
Moderate LTPA[†]				
Yes	258 (86.6)	183 (84.7)	75 (91.5)	0.127
Vigorous LTPA				
Yes	68 (22.7)	41 (18.9)	27 (32.9)	0.010
Total LTPA				
Yes	264 (88.3)	186 (85.7)	78 (95.1)	0.024
ACOG Guidelines[†]				
Meets	111 (37.1)	78 (35.9)	33 (40.2)	0.492
Pregnancy LTPA Intention				
Yes	238 (79.9)	168 (77.8)	70 (85.4)	
No	48 (16.1)	40 (18.5)	8 (9.8)	0.177
Depends	12 (4.0)	8 (3.7)	4 (4.9)	

*Chi-square p-values compare women who did and did not complete follow-up

[$] n=5 women did not report family income in the original interview

[†]LTPA= Leisure-time physical activity; ACOG=American College of Obstetrics and Gynecology; "Meets" ACOG Guidelines = original report of total LTPA ≥150 min/wk

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Table 6.2: Average LTPA* values and mean differences in originally reported and recalled values for moderate, vigorous, and total LTPA among women who completed follow-up (n=82)

	Original LTPA (min/wk)	Recalled LTPA (min/wk)	Original – Recalled LTPA (min/wk)
Moderate LTPA	131.1 ± 108.5	137.1 ± 152.1	-6.0 ± 175.5 (-620 to 420)
Vigorous LTPA	30.5 ± 59.6	26.9 ± 65.8	3.6 ± 71.5 (-420 to 210)
Total LTPA	161.6 ± 133.6	164.0 ± 179.1	-2.4 ± 193.6 (-605 to 435)

Value are means ± standard deviations (ranges)
* LTPA = Leisure-time physical activity

Table 6.3: Spearman correlations (r_s, p-value) between originally reported and recalled min/wk of moderate, vigorous, and total LTPA for the group as a whole and by participant subgroups

	Moderate LTPA[#]	Vigorous LTPA[#]	Total LTPA[#]
Total Group n=82	0.10 (0.35)	0.34 (<0.001)*	0.28 (0.02)*
Age at Interview			
18-<30 yrs (n=44)	0.16 (0.29)	0.17 (0.27)	0.20 (0.20)
30-<50 yrs (n=38)	0.02 (0.97)	0.55 (<0.001)*	0.32 (0.05)*
Parity			
Nulliparous (n=40)	0.19 (0.25)	0.39 (0.01)*	0.30 (0.06)
Parous (n=42)	0.02 (0.89)	0.23 (0.15)	0.22 (0.16)
Family Income			
< $50,000 (n=37)	-0.02 (0.91)	0.08 (0.63)	0.08 (0.64)
≥ $50,000 (n=45)	0.17 (0.27)	0.53 (<0.001)*	0.39 (0.01)*
BMI at Recall			
< 25 kg/m^2 (n=46)	0.21 (0.15)	0.37 (0.01)*	0.33 (0.03)*
≥ 25 kg/m^2 (n=36)	-0.03 (0.88)	0.14 (0.48)	0.11 (0.57)
ACOG Recs at Recall[$]			
Meets (n=43)	0.18 (0.24)	0.29 (0.08)	0.38 (0.01)*
Does not Meet (n=39)	-0.02 (0.93)	0.42 (0.01)*	0.07 (0.66)

[#] LTPA = Leisure-time physical activity
[$] "ACOG Recs at Recall" classifies women into meeting (≥150 min/wk) or not meeting (< 150 min/wk) ACOG recommendations based on their report of LTPA during the previous month at the time of recall
*p<0.05

Table 6.4: Categorical agreement between originally reported and recalled participation in moderate, vigorous, and total LTPA, and participation in ACOG recommended amounts of LTPA

	Original Report		Percent Agreement	Kappa Value
	Yes (n)	No (n)		
Moderate LTPA*				
Recall Yes	59	16	74%	0.015
Recall No	6	1		
Vigorous LTPA*				
Recall Yes	11	16	70%	0.183
Recall No	9	46		
Total LTPA*				
Recall Yes	64	3	79%	0.031
Recall No	14	1		
Meets ACOG Recommendations*				
Recall Yes	16	17	57%	0.117
Recall No	18	31		

*LTPA= leisure-time physical activity; "Meets ACOG Recommendations"= reports ≥ 150 min/wk of total LTPA

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CHAPTER SEVEN

SUMMARY AND RECOMMENDATIONS

SUMMARY OF RESULTS

The purposes of this dissertation were three-fold: to determine the effects of LTPA during pregnancy on offspring size at birth, to determine the effects of LTPA during pregnancy and child LTPA on child weight status at 3-9 years of age, and to determine the reliability of postpartum recall of LTPA during pregnancy. Using data from the POUCH study we found that maternal LTPA during pregnancy at or above recommended levels was associated with decreased odds of giving birth to an LGA infant (Chapter 3). Furthermore, using quantile regression, we were able to demonstrate that the effect of LTPA during pregnancy was limited to the upper quantiles of birth weight z-score such that participating at or above recommended levels reduced birth weight z-scores above the 0.65 quantile without causing a mean shift in the distribution. Due to the adverse maternal and child health effects associated with higher birth weight, these results may indicate a substantial health benefit for LTPA during pregnancy, without increased risk of SGA.

Beyond effects on offspring size at birth, we also sought to determine whether participation in LTPA during pregnancy was associated with weight status during childhood, while also considering child LTPA level (Chapter 5). Using a combined maternal/child LTPA variable within the POUCH cohort, we found that inactivity during pregnancy combined with either non-sedentary or sedentary child activity were associated with borderline significant increased odds of child obesity as compared to any LTPA during pregnancy combined with non-sedentary child activity. The highest odds of

child obesity were observed when both the mother and child were classified as inactive/sedentary. Thus it appears that both maternal LTPA during pregnancy and children's own LTPA level may be important in the development of child obesity.

Finally we used the MANCS pilot study cohort to examine reliability of recalling LTPA during pregnancy at 15-30 months postpartum (Chapter 6). Correlational analyses indicated moderate relationships between original and recalled reports of min/wk of vigorous and total LTPA, but relationships for moderate activity were non-significant. Older age, higher income, having a healthy weight, and participating in recommended amounts of LTPA at follow-up were associated with better recall ability for total LTPA. There were high percent agreements for original vs. recalled report of any moderate, vigorous, or total LTPA, and moderate percent agreement for meeting LTPA guidelines, but kappa values for all of these relationships were low. Overall, these results support moderate reliability for recalling LTPA during pregnancy. Thus, researchers may consider the use of historical recall of LTPA during pregnancy when prospective measurements are not feasible. However, larger sample sizes may be needed to counter variability due to misclassification and participant characteristics known to influence recall ability should be included in multivariate models.

Taken as a whole, our results indicate a role for maternal LTPA during pregnancy to affect not only offspring size at birth, but also weight status in early childhood when combined with child activity level. Our results provide preliminary evidence that maternal participation in LTPA may help to improve offspring health by normalizing size at birth and reducing odds of child obesity. While we had to rely on recalled LTPA data

within the POUCH study cohort, our results from the MANCS pilot study cohort indicate that postpartum recall of LTPA during pregnancy is moderately reliable.

RECOMMENDATIONS

Future research is needed to further test and refine our findings. Prospective studies with detailed measures of LTPA throughout pregnancy are needed to determine trimester-specific effects of LTPA on offspring size. This will help to refine recommendations for LTPA during pregnancy to maximize maternal and offspring health benefits. Future studies should also seek to incorporate objective and direct measures of child body size and LTPA participation, such as body fatness and accelerometry, so that combined influences of maternal LTPA during pregnancy and child LTPA participation on child body size can be more fully explored.

One of the advantages of using the POUCH cohort to evaluate our aims was that a wide range of recalled LTPA participation was present. Future prospective studies should seek to recruit samples of women with diverse LTPA participation so that dose-response relationships with offspring size can be evaluated. It is yet to be determined whether a minimal threshold amount of LTPA is needed to effect offspring size. Our results for Aim One indicated that LTPA participation at or above the ACOG recommended amount was associated with reduced BWz among the upper quantiles of the distribution, while participation in LTPA below this level was not associated with BWz. In contrast, our results for Aim Two indicated that participation in *any* LTPA during pregnancy combined with non-sedentary child activity reduced the odds of child obesity. Future studies with more exact measures of LTPA throughout pregnancy and of child body size may be able to delineate a more specific minimum threshold level of LTPA during

pregnancy needed to effect offspring size. As yet no study has determined a maximum threshold of LTPA participation that would begin to increase maternal/child health risks rather than benefits. This is likely due to the fact that few women choose to exercise vigorously throughout pregnancy, thus it is hard to gather generalizable data on the effects of vigorous LTPA.

Future studies should begin to examine the relationship of maternal LTPA during pregnancy with maternal/fetal biomarkers to test for biologically plausible pathways for the effects of LTPA during pregnancy on offspring size and other health outcomes. Our results provide evidence that maternal inactivity during pregnancy combined with either non-sedentary or sedentary child activity increases risk for child obesity. However, whether this relationship is the result of biological influences of LTPA during pregnancy on fetal development, or environmental influences on child behavior is still debatable. Possible biological effects could be evaluated by examining relationships between LTPA during pregnancy and fetal metabolic parameters. Examining relationships among LTPA during pregnancy, maternal postnatal behaviors, and child LTPA and dietary behaviors would help to determine how environmental influences also effects offspring size.

This dissertation focused on LTPA during pregnancy, and the vast majority of women in both cohorts reported participation in aerobic LTPA (i.e., walking). Future studies are needed to evaluate the influence of other types of LTPA, such as strength training or yoga, on birth outcomes and offspring size. It is also important to consider the contribution of other domains of physical activity, such as occupational and household-related physical activity. Due to the intermittent nature and varying intensity level of occupational and household-related activities, the effects of participating in these

domains of physical activity may be very different from the effects associated with LTPA participation.

Finally, we found moderate reliability for postpartum recall of LTPA during pregnancy using the MAQ compared to original LTPA questions based on the BRFS. It would be preferable to establish validity of recalling LTPA during pregnancy by using objective measures, such as accelerometry, throughout pregnancy. In the absence of accelerometry data, researchers should procure more detailed LTPA questionnaire data during pregnancy so that total volume of LTPA reported originally and at recall can be compared. The reliability of recalling other domains of physical activity during pregnancy also needs to be established to facilitate epidemiological studies examining outcomes associated with these variables.

The results of this dissertation set the stage for a line of inquiry further evaluating the effects of maternal LTPA during pregnancy on offspring size and health. Future study incorporating prospective, detailed measures of LTPA during pregnancy, child LTPA, and child size at birth through childhood will help to more specifically define the independent effect of LTPA during pregnancy on offspring size. If our results are confirmed, then future research may also seek to evaluate the efficacy of LTPA intervention programs during pregnancy to reduce risk for child obesity.