PHYSICAL ACTIVITY MEASURED EARLY IN PREGNANCY AND BIRTHWEIGHT- A STUDY FROM THE ARCH COHORT

By

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ABSTRACT

PHYSICAL ACTIVITY MEASURED EARLY IN PREGNANCY AND BIRTHWEIGHT- A STUDY FROM THE ARCH COHORT

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Excessive birthweight is a growing concern and challenge in current obstetrics, and has been associated with perinatal complications, such as shoulder dystocia, and long-term health complications such as type 2 diabetes. (1-3) Variation of birthweight measures used to describe excessive birthweight contributes to the lack of consensus in the literature. In addition, these measures do not allow for the study of the effect of Physical Activity (PA) at non-traditional points in the distribution. The effect of PA may not be found at mean birthweight estimates, but an effect may be present above the 70th percentile of birthweight z-scores standardized for infant sex and gestational age.(4) We hypothesized that women who performed 150 minutes or more of PA per week on average would have lower odds of delivering a neonate whose birthweight z-score was above the 70th percentile of the sample's birthweight z-score compared to the neonates of women who were sedentary. We also sought to replicate findings that birthweight z-score varies by PA category above the 70th percentile of birthweight z-score using a sample in which PA behavior data was collected prospectively.(4) We used data from the Archives for Research on Childhood Health cohort. We calculated birthweight z-score and trichotomized PA. We used multivariable logistic regression to model the association between PA measured early in pregnancy and birthweight z-score above the 70th percentile. This study did not support the hypothesis that the odds of delivering a neonate above the 70th percentile would be lower for women who performed 150 minutes or more of PA per week compared to the neonates women who were sedentary.

This thesis is dedicated to the families who participated in ARCH.
Without you, this work would not exist.

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KEY TO ABBREVIATIONS

ARCH	Archive for Research on Childhood Health
CI	Confidence Interval
DHHS	Department of Health and Human Services
HBW	High Birthweight
LGA	Large for Gestational Age
NHB	Non-Hispanic Black or African American
NHW	Non-Hispanic White or Caucasian
PA	Physical Activity
T2DM	Type 2 Diabetes Mellitus

INTRODUCTION

High Birthweight (HBW) has been described as a current challenge in obstetrics practice, and preventing birthweights in the high end of the distribution is an important step in controlling adverse pregnancy outcomes and chronic disease.(1)Adverse pregnancy outcomes can include complications such as shoulder dystocia (odds ratio: 2.4. 95% confidence interval [CI}: 1.6, 3.6), and neonatal hypoglycemia (odds ratio: 4.2. 95% CI: 3.3, 5.4).(2) Odds of type II diabetes mellitus (T2DM) may be increased in persons whose birthweight was greater than 4000 grams (odds ratio: 1.3. 95% CI: 1.0, 1.6). (3) A variety of definitions of HBW have been used across the literature, which has contributed to the debate about the relationship between Physical Activity (PA) and birthweight. (5-7) Measures of birthweight include mean birthweight (8), Large for Gestational Age (LGA)(7), HBW(9), and fetal growth ratio.(10) LGA, which highlights one end of the birthweight distribution, focuses only on the 90th percentile of birthweight and above. HBW is often defined as a birthweight greater than 4000 grams (see CDC Pediatric and Pregnancy Nutrition Surveillance System for surveillance definition: http://www.cdc.gov/pednss/what_is/pednss_health_indicators.htm). Nevertheless, prevention of birth weights in the extreme ends of the distribution is a public health priority; Healthy People 2020 has a goal of reducing the maternal mortality rate due to labor and delivery complications(11), some of which have been closely associated HBW pregnancy outcomes.(2, 12, 13) An association between birthweight greater than 4000 grams and excessive bleeding (odds ratio: 1.41. 95% CI: 1.37, 1.45), prolonged labor (odds ratio: 1.38. 95% CI: 1.35,1.41), cephalopelvic distortion (odds ratio: 2.42. 95% CI: 2.41, 2.45), and C-section delivery (odds ratio: 1.62. 95% CI: 1.61, 1.63).(12) Other important US public health goals include reducing obesity rates and diseases associated with obesity, such as T2DM and heart disease. (11) There is evidence that suggests these diseases are influenced by birthweight. Associations between birthweights and health problems associated with obesity, such as childhood obesity (14, 15), metabolic syndrome (16), T2DM(3, 17, 18), and cardiovascular disease(16), have been found. One study found for each kilogram increase in birthweight, childhood body mass index (BMI) increased by half a unit (95% CI: 0.47, 0.51). (15) The hazard ratio for metabolic syndrome in children who were born LGA was 2.2 (95% CI: 1.3, 3.8) when compared to children who were born average for gestational age. (19)

Mechanism of High Birthweight

Maternal glucose levels during pregnancy are associated with birthweight. (20-22) It has been shown that odds of LGA were 3.6 times higher for women whose fasting glucose was greater than 130 mg/dl when compared to women whose fasting glucose was less than 99 mg/dl. (21) Gestational diabetes and chronic diabetes have both been associated with high birthweight outcomes, and this association has been noted for decades.(23, 24) Glucose crosses the placenta and the fetus responds by producing insulin.(25) Insulin in the fetal environment promotes growth, and it has been proposed that in the presence of excess glucose, the fetus will produce more insulin than a fetus exposed to optimal glucose, thereby promoting excessive growth.(26-28) Effective maternal glucose control, achieved through dietary advice, medication, and glucose monitoring during pregnancy has been demonstrated as an important step toward disrupting this pathway to high birthweight outcomes in clinical trials.(29, 30) One trial demonstrated a 100 gram reduction in mean birthweight through control of mild gestational diabetes.(29) Importantly, adverse delivery outcomes, including serious perinatal complications and shoulder dystocia, were reduced in glucose intervention groups in some of these trials, which demonstrated that the interruption of the maternal glucose-fetal insulin growth pathway is important for reducing morbidity and mortality associated with high birthweight.(29, 31) PA during pregnancy may be an effective intervention to help prevent women from delivering pathologically large infants, but few trials have tested this. A 2012 Cochrane Review of PA trials and perinatal outcomes found only two trials that analyzed exercise interventions and macrosomia, defined as birthweight greater than 4000 grams.(32) The estimated effect size was modest and statistically not significant.(32)

Risk Factors that May Confound or Modify the Relationship between PA and Birthweight

Important risk factors associated with high birthweight include overweight or obese pre-pregnancy BMI classification (23, 33, 34) , maternal height (23, 33), parity greater than two (23, 33), and excessive gestational weight gain.(35, 36) Some of these risk factors are modifiable, while others are not, but effective targeted interventions for reducing the associated risk are essential. Maternal pre-pregnancy BMI is believed to affect birthweight through modification of placental hormones that regulate metabolism and delivery of nutrients to the fetus, such as insulin like growth factor.(37) One study found that mothers who weighed 80 or more kilograms had a 1.9 (95% CI: 1.7, 2.2) fold increase in odds of giving birth to an infant who weighed more than 4000 grams. (33) Maternal height is believed to influence birthweight through genetic pathways(38), but the relationship between fetal growth ratio and PA varies significantly by maternal height.(10) Mothers whose height was between 1.81 and 1.9 meters had an increased odds of delivering an infant greater than 4000 grams of 1.2 (95% CI: 1.1, 1.3), while mothers whose height was in excess of 1.9 meters had odds of delivering a HBW infant of 1.4 (95% CI: 1.2,1.5).(33) Excessive gestational weight gain has been associated with increased risk of delivering high birthweight infants (36, 39), but an exact mechanism has not been elucidated. One study found that regardless of pre-pregnancy BMI classification, excessive gestational weight gain was associated with greater than two-fold odds of delivering a HBW infant.(36) Glycemic load during pregnancy has been associated with both excessive gestational weight gain and high birthweight outcomes, which suggests a nutritional pathway associated with maternal glucose levels.(40) Maternal education, used as a proxy for socio-economic status, has been shown to be associated with birthweight, but a biological mechanism linking the two has not been elucidated.(23, 33)

Physical Activity and Pregnancy

PA during a healthy pregnancy has been recognized as an asset to both mother and fetus; the United States Department of Health and Human Services (DHHS) recommends healthy pregnant women engage in at least 150 minutes of moderate PA per week.(41) The literature has demonstrated that PA during pregnancy does not increase the risk of delivering a low birthweight baby.(42-46) In non-pregnant populations, PA has been demonstrated to be effective at increasing insulin sensitivity; accumulated daily PA has a direct and positive effect on insulin sensitivity, and that this process may be similar in pregnant women.(47, 48) One study showed that moderate PA and vigorous PA had a positive impact on insulin sensitivity in non-pregnant women (beta coefficient for moderate PA: 0.08. beta coefficient for vigorous PA: 0.22. p-value for trend: 0.006).(47) Modifiable risk factors for high birthweight, such as excessive gestational weight gain, may also be positively impacted by PA.(49, 50) It has been observed that the fetal growth ratio of the offspring of active tall women was similar to the fetal growth ratio of the offspring of both active and inactive shorter women, while inactive taller women delivered offspring with statistically significant higher fetal growth ratios than inactive shorter women, active shorter women, and active taller women, which suggests PA may modify the relationship between maternal height and birthweight.(10)

Physical Activity and Birthweight

It has been proposed that PA can be leveraged to prevent high birthweight outcomes; however, results from trials have shown mixed effects. Most trials utilized a composite outcome, though one trial specified fetal macrosomia, one trial specified LGA, and one specified mean birthweight as primary endpoints.(8, 49, 51) The trial that specified macrosomia, defined as birthweight greater than 4000g, found no association between birthweight and the PA program that was tested.(8) A second trial stratified analyses by pre-pregnancy BMI, but found no significant difference between LGA offspring in the intervention groups regardless of pre-pregnancy BMI.(49) One trial found PA reduced birthweight, but only in mothers who had gestational diabetes (mean difference: 302 grams, p-value = 0.02).(51) A fourth trial tested the effect of a lifestyle counseling intervention on birthweight; the intervention included counseling on PA, and found a 100 gram reduction in mean birthweight in the intervention group. (52) Observational studies have yielded mixed results for the relationship of PA and birthweight. (4, 6, 7, 9, 10, 34, 48, 53-55). Studies that have found inverse associations between birthweight and PA during pregnancy frequently dichotomize birthweight, using measures such as birthweights greater than 4000 grams, or LGA. Large observational studies, such as the Danish National Birth Cohort and the Norwegian Mother and Baby Cohort (MoBa), have demonstrated no difference in mean birthweight when comparisons between exercising women's infants were made to non-exercising women, but have found PA reduces risk for LGA.(7, 9) A study from the Danish National Birth Cohort found no difference in mean birthweight, but the hazard ratio for delivering LGA was 0.93 (95% CI: 0.88, 0.98).(7) Other studies have found PA during pregnancy exerts no effect on birthweight, or has less effect than modifying pre-pregnancy risk factors like overweight or obese BMI.(34, 56) Challenges to interpreting these study results include varying measures of birthweight, including grams(34), fetal growth ratio(10), and birthweight z-score(4), as well as different definitions of high birthweight, including LGA and a cut point of greater than 4000 grams.(7, 9) Variation in the timing of PA assessment methods is another challenge to interpreting the results of these studies, with the timing of assessment ranging from prospective to retrospective.(4, 7, 9, 10, 34, 46) Many prospective studies have assessed PA during the second or third trimester of pregnancy, or during both trimesters; others have not reported the timing of data collection for PA.(34, 53, 57) One study found PA in the first trimester was associated with lower risk of high birthweight, but it was a small investigation conducted in urban dwelling Indian women and may not be generalizable to the United States.(58) Women in this study who spent the most time doing physical activity had increased odds of delivering an infant in the lowest tertile; women were 1.6 times (95% CI: 1.0,2.4) more likely to deliver in the lowest tertile compared to women who performed the least physical activity.(58)

In spite of variation across the literature, association between PA and birthweight is most likely captured in the extreme ends of the birthweight distribution. Studying the variation in birthweight at different cut-points in the high end of the distribution, such as the 70th percentile, may help further describe the association between PA and HBW.

Gaps in Knowledge

Mudd et al. suggest that birthweight may be impacted by leisure time PA during pregnancy above the 70th percentile of the birthweight z-score distribution, however, this study used retrospective PA recall three to nine years after the study pregnancy.(4) It remains unknown if this relationship between PA and birthweight z-score holds in a cohort characterized by prospectively collected PA data. It also remains unclear if the timing of PA during pregnancy is an important factor in the relationship between PA and birthweight. Additionally, it is unknown if this relationship holds for all daily PA, as opposed to leisure time only PA.

Objective

Our objective was to describe the association between PA measured at a mean gestational age of 13.8 weeks and birthweight z-score above the internally calculated 70th percentile. (4)

METHODS

We obtained data from the Archive for Research on Childhood Health (ARCH). Briefly, ARCH is a biotrust which prospectively collects maternal questionnaire data, birth certificate information, hospital discharge data, and biological samples as early as four weeks into pregnancy. Women are recruited from three prenatal care clinics in the Lansing, MI area, and mother and child dyads are followed for at least five years post-birth. Mothers must be at least 18 years of age at enrollment and speak English. Mean gestational age at enrollment for the entire cohort is 13.2$\pm$ 6.3 weeks, but women are eligible to enroll at any time prior to birth. The mean gestational age at enrollment for the study sample was 13.8$\pm$ 6.3 weeks. The Michigan State University Institutional Review Board for Human Subjects Research approved this study.

Conceptual Model

The conceptual model for this study was based on work by Mudd et al. Their study used quantile regression, and identified the 70th percentile of birthweight z-score to be the point in the distribution where birthweight z-score differed by retrospectively measured leisure time PA.(4) For this study, our approach was to dichotomize the sample's birthweight z-scores at the 70th percentile. We used logistic regression to estimate the odds ratio for birthweight z-score above the 70th percentile for prospectively measured PA categories. Categories were a) active, but not meeting Department of Health and Human Services recommendation of 150 minutes of moderate activity per week (here after referred as active, not meeting recommendation), b) active, meeting Department of Health and Human Services recommendation of 150 minutes per week (here after referred to as active, meeting recommendations), and C) women who reported performing no PA (here after referred to as sedentary). PA was not limited to leisure time in this study, but could include PA attributable to work or leisure.

Inclusion

For this analysis, we included mother and child dyads if they had recorded PA data as well as birthweight and gestational age data recorded for the calculation of birthweight z-score. Additionally, subjects included had to have been enrolled in ARCH during the index pregnancy; the gestational age at enrollment had to be plausible, and were limited to gestational age at enrollment between 1 and 42 weeks. Subjects with gestational age at enrollment greater than 42 weeks were excluded. Subjects must also have had complete data available for covariates, including maternal race, maternal age, maternal height, pre-pregnancy BMI, parity status, educational attainment, household income, and maternal smoking prior to or during pregnancy. Dyads with one of the above variables missing were excluded (see Figure 1).

Exposure

Our exposure of interest was variable PA measured at intake interview for the ARCH cohort. ARCH investigators assessed PA by using questions modified from the 2009 Behavior Risk Factor Survey.(59) Pregnancy PA was ascertained at the recruitment interview using the following questions:

- During the past month, did you do any moderate activities for more than ten minutes that caused a small increase in your breathing and heart rate?
    - If yes, how many days a week do you usually do these moderate activities?
    - How much time do you usually spend doing these moderate activities in one day?
- During the past month did you do any vigorous activities for more than ten minutes that caused a small increase in your breathing and heart rate?
    - If yes, how many days a week do you usually do these vigorous activities?
    - How much time do you usually spend doing these vigorous activities in one day?

The number of moderate PA minutes per session was multiplied by the number of moderate PA sessions per week reported to calculate the number of moderate PA minutes per week. The number of vigorous PA minutes per session was multiplied by the number of vigorous PA sessions per week to calculate the number of vigorous PA minutes per week. The number of vigorous minutes performed per week was then doubled to roughly equate vigorous and moderate minutes of PA. This calculation assumes the intensity of vigorous activity is approximately twice that of moderate activity. The total number of minutes usually performed per week was calculated by adding the number of moderate PA minutes per week and the doubled number of vigorous PA minutes performed per week.

Outcome

Our outcome was birthweight z-score dichotomized at the 70^{th} percentile of the sample. We derived birthweight z-score from the birthweight in grams reported on the birth certificate subtracted from the United States population mean birthweight for gestational age and sex, and divided by the United States population standard deviation proposed by Talge, Mudd et al.(60) The sample's 70^{th} percentile of birthweight z-score was calculated, and a dichotomous variable was created that classified infants as at or below the 70^{th} percentile or above it.

Covariates

We calculated pre-pregnancy body mass index (weight in kg/height in meters, squared) and women were categorized into one of three groups: less than 25 kg/m^2, 25-29.9 kg/m^2, and 30 kg/m^2 or greater. The range of pre-pregnancy BMI was 16.5 - 56.5. We categorized maternal age in five groups: Less than 20 years of age, 20-24 years of age, 25-29 years of age, 30-34 years of age, and 35 years of age or older. We categorized maternal height into women less than the 75^{th} percentile of height, women between the 75^{th} and 90^{th} percentile, and women above the 90^{th} percentile, based on the United States reference for women over 20 years of age.(61) We categorized marital status as unmarried, unmarried but living with baby's father, and married. We categorized parity as nulliparous, primiparous, and multiparous. Due to small numbers, we divided maternal race into three categories: Non-Hispanic White or Caucasian (NHW), Non-Hispanic Black or African American (NHB), and Other Race or Ethnicity, including Latina. We dichotomized household income into less than US$25,000 per year versus US$25,000 a year or more. We used covariates that were collected from the intake interview, except maternal smoking before or during pregnancy, parity and maternal age at birth, which were collected from birth certificate data.

Statistical Analysis

We conducted univariate analysis of frequencies of the birthweight z-score above the 70th percentile, PA categories, and the following covariates of interest: pre-pregnancy BMI, maternal age, maternal height, parity, maternal race/ethnicity, and household income. We considered excessive gestational weight gain a mediator and did not include it in modeling. Bivariate analysis for the outcome of greater than the 70th percentile birthweight z-score and the exposure of active, meeting recommendations, active not meeting recommendation, and sedentary were conducted using frequencies and chi-square tests. We assessed frequency tables of covariates and PA with chi-square tests. We used logistic regression to assess the impact of PA on birthweight z-score by modeling the probability of having a birthweight greater than the 70th percentile given PA status, while controlling for the following covariates: maternal height, maternal age, household income, maternal race, maternal education, parity status, pre-pregnancy BMI, smoking status before or during pregnancy, and marital status. We used backward selection to reduce the model, with a p-value of 0.2 set as the threshold for retention. After backward selection, we tested interactions among retained variables, and used backward selection to determine which interaction terms to retain. All analyses were performed with SAS 9.4; the primary procedure was Proc Logistic (SAS Institute, Cary, NC).

Post Hoc Power Analysis

We conducted a post hoc power analysis to determine the power detecting a difference in birthweight z-score above the 70th percentile in women who reported active, meeting recommendations PA and women who were classified as sedentary. Analysis was performed with Stata 13. We set the alpha level at $p \leq 0.05$. Calculation for power was calculated from a sample size of 331, the control proportion of 21.5% of births greater than the 70th percentile, and an odds ratio of 1.2.

RESULTS

At the time of analysis (October 2016), ARCH had enrolled 841 women. Of the 841 observations, 223 observations were missing birthweight z-score. Of the remaining 618 observations, 276 did not have data available for PA. Covariates were missing for 11 observations, so the final model included 331 women (Figure 1). Median gestational age at enrollment was 13.8 weeks, which was not different from the gestational age at enrollment of women not included. Observations included in the sample varied significantly from those that were excluded (Table 1) by maternal age (p-value <0.0001), marital status (p-value = 0.004), household income (p-value = 0.007), and maternal smoking status before or during pregnancy (p-value <0.0001). Table 2 shows the distribution of the outcome, birthweight z-score, the main exposure, PA performed during pregnancy, and selected covariates. Overall, 43.2% of the sample was classified as sedentary, 25.7% was classified as active, not meeting recommendation, and 31.1% was classified as active, meeting recommendation. More than half the sample was classified as overweight or obese prior to pregnancy, while 44.1% of the sample had a pre-pregnancy BMI of 25 kg/m^2 or lower. NHW women comprised 53.4% of the sample, while NHB women comprised 25.7% and women who reported another race or ethnicity, including Latina, comprised 20.9% of the sample. 48.3% of the sample was under the age of 25, while 27.8% were 25 to 29 years of age. Mothers age 30 and older made up 24.9% of the sample. Women whose height was less than the US 75^{th} percentile made up 64.4% of the sample. Women whose height was between the 75^{th} and 90^{th} US percentile made up 19.9% of the population, and women whose height was greater than the US 90^{th} percentile accounted for 15.7% of the sample. In this sample, 40.5% were nulliparous, 31.4% were primiparous, and 28.1% were multiparous. More than 70% of the sample participants were unmarried at the time of the interview, 36.9% were unmarried but living with the baby's father, while 37.2% reported being unmarried; 26.0% of the sample was married at the intake interview. The majority of the sample, 72.5%, lived in households with incomes of less than US$25,000 per year. About 50% of the sample had at least some college education, 18.3% did not finish high school, while 30.2% had a high school diploma or GED. The majority of the sample, 69.2%, did not smoke prior to or during pregnancy.

Table 3 gives the frequencies for the covariates by PA status. There were few differences across PA groups. PA performed during pregnancy was not associated with birthweight z-score; however, key covariates that did show a significant difference in frequency of PA status were maternal race (p-value =0.0005), marital status (p-value = 0.0003), household income (p-value = 0.0003), and maternal education (p-value= 0.04). Table 4 gives the results of bivariate analysis of the covariates by birthweight z-score status. Frequency of birthweight z-score above the 70^{th} percentile was significantly different across maternal race (p-value= 0.003) and maternal height status (p-value = 0.02).

Table 5 provides the beta estimates of the adjusted logistic regression modeling the probability of a birthweight z-score above the 70^{th} percentile given PA status. The final model was adjusted for maternal height, and maternal race and ethnicity, pre-pregnancy BMI, smoking before or during pregnancy, and marital status. Table 6 shows the odds ratio for birthweight z-score greater than the 70^{th} percentile. For the active, meeting recommendation women compared to sedentary women was 1.1 (95% CI: 0.6, 2.0) when holding all other variables constant, but was not statistically significant. The odds ratio for birthweight z-score for active, not meeting recommendations women compared to sedentary women was 1.3 (95% CI: 0.7, 2.4) when holding all other variables constant and was not statistically significant.

Birthweight z-score above the 70^{th} percentile did vary by maternal height when holding all other variables constant. For mothers whose height was between the 75^{th} percentile and the 90^{th} percentile for US women 20 years and older, there was a 2.2 fold increase in odds of delivering an infant whose birthweight z-score was greater than the 70^{th} percentile (odds ratio: 2.2 [95% CI: 1.2, 3.9]). Mothers whose height was greater than the 90^{th} percentile did not show a statistically significant difference in odds of delivering an infant greater than the 70^{th} percentile of birthweight z-score. Mothers who reported being NHB had a 50% reduction in odds of delivering an infant with a birthweight z-score above the 70th percentile (0.5 [95% CI: 0.2, 0.9]). The other covariates were not significantly associated with birthweight z-score. The c-statistic was 0.66 indicating the model was a poor predictor of birthweight z-score above the 70th percentile.

Results from the post hoc power analysis showed the power to detect a difference was 13%, based on a proportion in the reference group (sedentary women) of 41.3%, an odds ratio of 1.2, and a sample size of 331.

DISCUSSION

These results did not support the hypothesis that PA measured early in pregnancy and meeting the DHHS recommendations of 150 minutes per week performed during pregnancy will impact birthweight above the 70th percentile. In the literature, PA measured at multiple time points or after pregnancy is associated with a lower probability of delivering infants greater than 4000 grams, or who are LGA.(4, 7, 9) Multiple measures or recalled measures of PA may be representative of PA across pregnancy. This study used one measure of PA taken at a mean of 13.8 weeks gestation at enrollment. The early pregnancy timing of the interviews does not capture PA over the course of the entire pregnancy. The cumulative effect of PA across pregnancy may be necessary for affecting birthweight; this needs to be tested in longitudinal cohort studies that take repeated measures of PA across pregnancy with a diverse sample of women. Perkins et al used multiple time points to assess the relationship between PA and fetal growth ratio (birthweight/United States median birthweight for sex, gestational age, and race), but was limited to a sample focused on White, college educated women.(10) Further research with a diverse sample to allow generalizability is an important next step.

The measure of PA did not discern leisure time from work associated PA; work associated PA has been associated with small for gestational age, while leisure time PA has not.(62) It is possible that without separating the two, the effect of work and the effect of leisure time PA may cancel each other out. Compared to self-reported leisure time PA data from the 2000 Behavioral Risk Factor Survey, more women in this sample reported sufficient PA levels (31% of this sample versus 15%).(63) This study allowed women to include work associated PA, which could account for the higher prevalence of PA compared to the national estimates presented by Evenson et al. However, given the allowance for inclusion of work physical activity, the proportion of women in this sample who reported no physical activity was 43.2%, which is slightly higher than the proportion (38.8%) reported by in the non-subcohort women who recalled their PA three to nine years after pregnancy in the study by Mudd et al.

(4) Different measures of PA may contribute to this difference, but there may be other differences between the samples of the two studies that may be equally or more important. This highlights the challenge of consistently and accurately measuring PA using self-report.

Maternal height between the US 75th and 90th height percentile for women over age 20 had a significant odds ratio of 2.2 (95% CI: 1.2, 3.9). This relationship did not demonstrate an interaction with PA. This is different from the results of a recent study of the relationship between PA level and fetal growth ratio.(10) The authors found the relationship between PA and fetal growth ratio to be most prominent in the tallest women in the study.(10) The study used accelerometry and PA diaries to ascertain the relationship between daily PA during pregnancy and fetal growth ratio. Measures of PA were collected over the entire day, made at 20 and 32 weeks gestation, and provided a range of PA levels that provided sufficient variation to detect differences.(10)

Women who reported NHB race were 50 % less likely to deliver a neonate with birthweight z-score above the 70th percentile compared NHW women (OR: 0.5, 95% CI: 0.2, 0.9). The pattern of NHB women having smaller babies at term has been noted elsewhere.(64) Women who reported another race or ethnicity, including Latina, did not have significantly different odds of delivering an infant above the 70th percentile of birthweight z-score compared to NHW women. Interestingly, other covariates that typically predict differences in birth weight, such as maternal education, household income, parity, smoking status before or during pregnancy, and marital status, did not have significant associations with birthweight z-score in this analysis.

Limitations of this study include the sample; women for whom data were collected early in the ARCH recruitment period did not report PA; thus almost three hundred women were not available for analysis in this study. Women who did not report PA at their initial interview were also excluded from this analysis. Along with this, data collection for ARCH is ongoing, and birth certificate data were not yet available for 223 women, reducing the available sample size from 841 births to 342 births. Post hoc analysis shows these women are significantly different from the women who did not meet inclusion criteria by important variables including maternal smoking status before or during pregnancy, marital status, and household income. The ARCH cohort was recruited from a limited geographic area, and is not necessarily generalizable to all populations. It is possible the recruitment strategy for ARCH generated a sample too similar to make meaningful comparisons of PA during pregnancy.

This study has many strengths. Prospective ascertainment of PA is important for accuracy.(4) The ARCH protocol collects PA data at the initial enrollment interview, which is administered prior to birth. ARCH collects data from multiple sources, allowing for more complete data collection, and the ability to check for mistakes across sources. We used birthweight z-score for our outcome, which controls for sex and gestational age, which allowed us to use all gestational ages at birth, instead of limiting the analysis to infants born at term.

This analysis differed significantly from the work by Mudd et al. in terms of timing of PA assessment and ascertainment of PA.(4) Data were prospectively collected in this study. A different analysis was also conducted to assess the association between birthweight z-score above the 70th percentile.(4) This analysis used a dichotomized variable that divided the entire sample at the 70th percentile regardless of PA level. The analysis from Mudd et al. used quantile regression, which quantifies the difference between the birthweight z-score at the 70th percentile for women who were active and meeting PA recommendations, and compares them to the women who were not meeting PA recommendations.(4) This is a subtle difference, but one that is important for interpreting the results of this study. Quantile regression was attempted for this study, but the small sample size limited the ability to test the adjusted model.

CONCLUSIONS

This study does not support the hypothesis that PA performed early in pregnancy is associated with reduced odds of birthweight greater than the 70th percentile. Measuring PA in a sample that encompasses a wide variety of PA, and follows the participants across pregnancy may be more informative for studying the relationship between PA and birthweight outcomes. Determining the longitudinal impact of PA on birthweight in diverse populations is an important step in determining the ability for PA to reduce risk of HBW outcomes.

APPENDIX

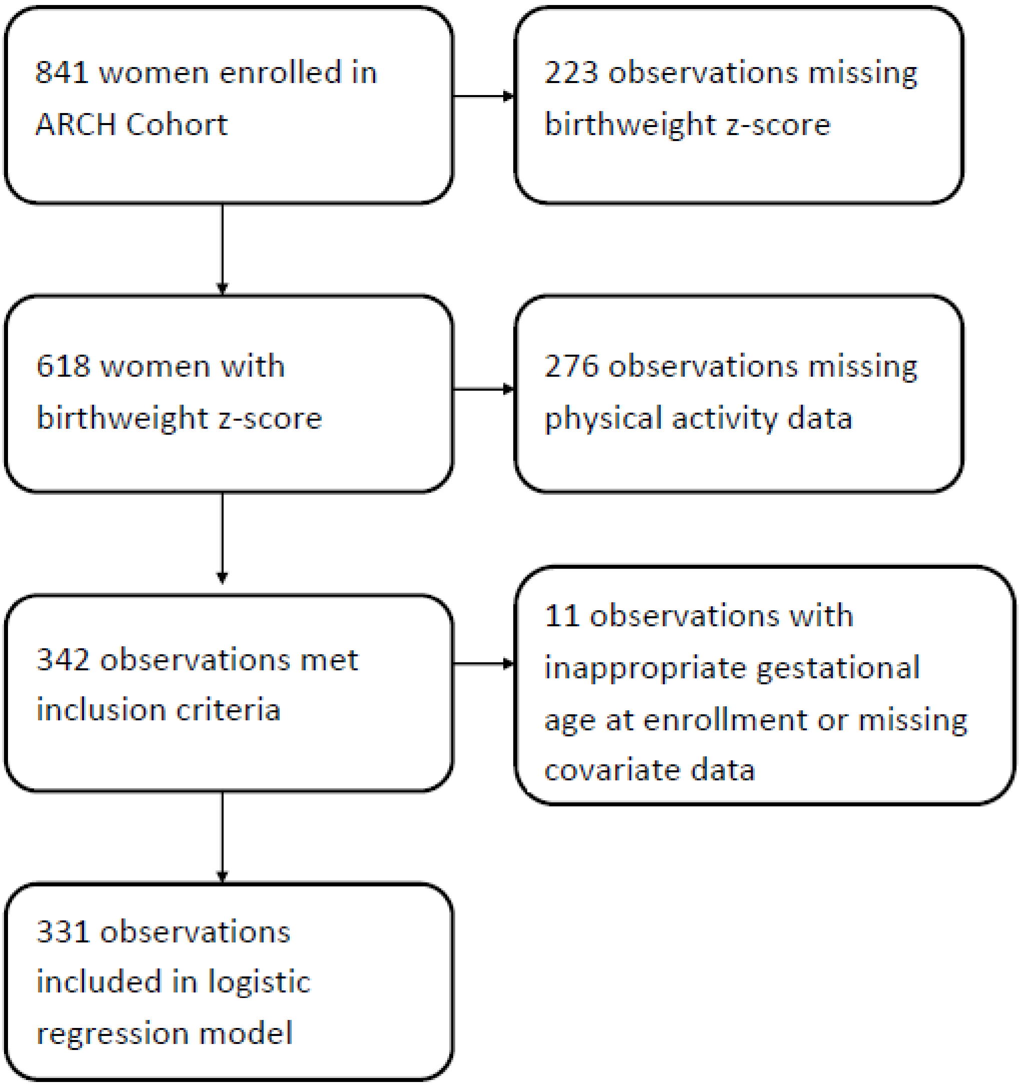

Figure 1: Flow chart of eligibility of subjects in the ARCH Cohort for analysis. Observations included in analysis based on inclusion criteria.

Table 1. Distribution of variables by included and excluded subjects[*], ARCH Cohort 2010-2015

Variable	Included	Percent	Excluded	Percent	Chi-Square	p-Value
BMI[b] Category						
Less than 25	147	17.5	241	28.8	0.8	0.7
25-29.9	86	10.3	123	14.7		
30 or Greater	98	11.7	143	17.1		
N = 838						
Maternal Race						
NHW	177	21.4	276	33.3	0.8	0.7
NHB	85	10.3	114	13.8		
Other including Latina	69	8.3	108	13.3		
N = 829						
Maternal Age						
<25 Years	160	19.0	363	43.2	45.9	<0.0001
25-29 Years	92	10.9	76	9.0		
30-34 Years	50	6.0	51	6.1		
Greater than 35 Years	29	3.5	20	2.4		
N = 841						
Maternal Height						
At or Below 1.67 meters	213	25.3	353	42.0	2.5	0.3
Between the 1.67 and 1.71 meters	66	7.9	93	11.1		
Above 1.71 meters	52	6.2	64	7.6		
N = 841						
Parity Status[a]						
Nulliparous	134	21.7	119	19.3	0.2	0.9
Primiparous	104	16.8	85	13.8		
Multiparous	93	15.1	83	13.4		
N = 618						
Marital Status						
Married	86	10.3	182	21.7	10.8	0.004
Unmarried, Living with Baby's Father	123	14.7	145	17.3		
Unmarried	122	14.6	180	21.5		
N = 838						
Household Income						
Under US$25,000	240	29.7	303	37.5	7.4	0.007
US$25,000 or Higher	91	11.3	175	21.6		
N = 809						
Maternal Education						
Did not Finish High School	60	7.3	71	8.6	4.4	0.2

Table 1. (cont'd)

High School Graduate or GED	100	12.1	169	20.4		
Some College	112	13.5	152	18.4		
College Graduate or Higher	59	7.1	104	21.0		
N = 827						
Maternal Smoking Before or During Pregnancy[a]						
Yes	102	16.6	47	7.6	17.1	<0.0001
No	229	37.2	238	38.6		
N = 616						
Gestational Diabetes[ac]						
Yes	10	1.6	6	1.0	Fisher's Exact Test	0.6
No	320	51.9	280	45.4		
Total = 594						
Gestational Hypertension[ac]						
Yes	22	3.6	10	1.6	Fisher's Exact Test	0.02
No	308	49.9	276	44.7		
Total = 594						
Gestational Age at Enrollment	Mean	Std Dev	Mean	Std Dev	Mean Diff	p-value
	13.2	6.3	13.8	6.5	0.6	0.2
Sample Size/ Equality of Var Test	288		327		Folded F	0.7

Abbreviations: ARCH, Archive for Research of Childhood Health; PA, physical activity; NHW, non-Hispanic/Latina White; NHB, non-Hispanic/Latina Black; BMI, body mass index; kg, kilogram; m, meter; diff, difference; var, variance.

[*] To be included subjects had to have complete data for birthweight, sex of neonate, gestational age at birth, physical activity, and covariates.

[a] Covariates obtained from birth certificates. Subjects whose birth certificate data had not yet been received were excluded.

[b] Weight (kg)/height (m)^2

[c] Not included in covariates necessary for inclusion

Table 2. Distribution of Variables of subjects, ARCH Cohort 2010-2015

N= 331

Variable	Frequency	Percent
Birthweight Z-Score[a]		
Below 70th Percentile	234	70.7
Above 70th Percentile	97	29.3
Physical Activity Category		
Sedentary	143	43.2
Inadequate	85	25.7
Adequate	103	31.1
BMI[b] Category		
Less than 25	147	44.1
25-29.9	86	26.0
30 or Greater	98	29.6
Maternal Race		
Non-Hispanic White	177	53.4
Non-Hispanic Black or African American	85	25.7
Other including Hispanic and Latina	69	20.9
Maternal Age		
Less than 25 Years	160	48.3
25-29 Years	92	27.8
30-34 Years	50	15.1
Greater than 35 Years	29	8.8
Maternal Height		
At or Below 1.67 meters	213	64.4
Between the 1.67 and 1.71 meters	66	19.9
Above 1.71 meters	52	15.7
Parity Status		
Nulliparous	134	40.5
Primiparous	104	31.4
Multiparous	93	28.1
Marital Status		
Married	86	26.0
Unmarried, Living with Baby's Father	122	36.9
Unmarried	123	37.2
Household Income		
Under US$25,000	240	72.5
US$25,000 or Higher	91	27.5
Maternal Education		
Did not Finish High School	57	18.3
High School Graduate or GED	94	30.2
Some College	105	33.8

Table 2. (cont'd)

College Graduate or Higher	55	17.7
Maternal Smoking Before or During Pregnancy		
Yes	102	30.8
No	229	69.2
Gestational Diabetes[c]		
Yes	10	3.0
No	320	96.7
Total	330	
Gestational Hypertension[c]		
Yes	22	6.7
No	308	93.1
Total	330	

Abbreviations: ARCH, Archive for Research of Childhood Health; PA, physical activity; NHW, non-Hispanic/Latina White; NHB, non-Hispanic/Latina Black; BMI, body mass index; kg, kilogram; m, meter; diff, difference; var, variance.

[a] Birthweight z-score was calculated using the United States' gestational age and sex specific means and standard deviations. The sample's 70th percentile was calculated and used as the cut-point.

[b] Weight (kg)/height $(m)^2$

[c] Not included in covariates necessary for inclusion because they are mediators and were not intended to be used in model.

Table 3. Bivariate Distribution of Birthweight Z-Score[a] and Covariates by Physical Activity, ARCH Cohort 2010-2015

	Physical Activity Category						Chi-Square	P-Value
	Sedentary		Active, less than 150 minutes		Active, 150 minutes or more			
Birthweight Z-Score								
Below 70th Percentile	106	74.1	57	67.1	71	68.9	1.5	0.5
Above 70th Percentile	37	25.9	28	32.9	32	31.1		
Pre-Pregnancy BMI[b] Category								
Less than 25	65	45.5	39	45.8	43	41.7	6.7	0.2
25-29.9	37	25.9	16	18.8	33	32.0		
30 or Greater	41	28.7	30	35.3	27	26.2		
Maternal Race								
Non-Hispanic White	59	41.3	54	63.5	64	62.1	20.2	0.0005
Non-Hispanic Black or African American	47	32.9	22	25.9	16	15.5		
Other including Latina	37	25.9	9	10.6	23	22.3		
Maternal Age								
Less than 25 Years	83	58.0	40	47.1	37	35.9	13.4	0.04
25-29 Years	29	20.3	25	29.4	38	36.9		
30-34 Years	19	13.3	14	16.5	17	16.5		
Greater than 35 Years	12	8.4	6	7.1	11	10.7		
Maternal Height								
At or Below 1.67 meters	96	67.1	57	69.5	60	58.3	3.2	0.5
Between the 1.67 and 1.71 meters	27	18.9	17	20.0	22	21.4		
Above 1.71 meters	20	14.0	11	12.9	21	20.4		
Parity Status								
Nulliparous	60	42.0	38	44.7	36	35.0	3.2	0.5
Primiparous	42	29.4	28	32.9	34	33.0		
Multiparous	41	28.7	19	22.4	33	32.0		
Marital Status								
Married	25	17.5	33	38.8	28	27.2	21.2	0.0003
Unmarried, Living with Baby's Father	49	34.3	26	30.6	47	45.6		
Unmarried	69	48.3	26	30.6	28	27.2		
Household Income								
Under US$25,000	120	83.9	55	64.7	65	63.1	16.5	0.0003
US$25,000 or Higher	23	16.1	30	35.3	38	36.9		

Table 3. (cont'd)

Maternal Education								
Did not Finish High School	36	25.2	10	11.8	14	13.6	13.4	0.04
High School Graduate or GED	47	32.9	26	30.6	27	26.2		
Some College	42	29.4	30	35.3	40	38.8		
College Graduate or Higher	18	12.6	19	22.4	22	21.4		
Maternal Smoking Before or During Pregnancy								
Yes	42	29.4	23	27.1	37	35.9	2	0.4
No	101	70.6	62	72.9	66	64.1		
Gestational Diabetes[c]								
Yes	3	2.1	5	6.0	2	1.9	Fisher's Exact Test	0.2
No	140	97.9	79	94.0	101	98.1		
Gestational Hypertension[c]								
Yes	8	5.6	9	10.7	5	4.9	Fisher's Exact Test	0.2
No	135	40.8	75	89.3	98	95.1		

Abbreviations: ARCH, Archive for Research of Childhood Health; PA, physical activity; NHW, non-Hispanic/Latina White; NHB, non-Hispanic/Latina Black; BMI, body mass index; kg, kilogram; m, meter; diff, difference; var, variance.

[a] Birthweight z-score was calculated using the United States' gestational age and sex specific means and standard deviations. The sample's 70th percentile was calculated and used as the cut-point.

[b] Weight (kg)/height (m)^2

[c] Not included in covariates necessary for inclusion because they are mediators and were not intended to be used in model.

Table 4. Bivariate Distribution of Physical Activity and Covariates by Birthweight Z-score[a], ARCH Cohort 2010-2015

	Birthweight Z-Score					
Variable	At or Below 70th Percentile		Above 70th Percentile		Chi-Square	P-value
Physical Activity Category						
Sedentary	106	45.3	37	38.1	1.5	0.5
Active, did not meet recommendation	57	24.4	28	28.9		
Active, did meet recommendation	71	30.3	32	33.0		
Pre-Pregnancy BMI[b] Category						
18.5-24.9	111	47.7	36	37.1	3.6	0.2
25-29.9	55	23.5	31	32.0		
30 or Greater	68	29.1	30	30.9		
Maternal Race/ Ethnicity						
Non-Hispanic White	116	49.6	61	62.9	6.8	0.03
Non-Hispanic Black	69	29.5	16	16.5		
Other, Including Hispanic and Latina	49	20.9	20	20.6		
Maternal Age						
Less than 25 Years	117	50.0	43	44.3	1.4	0.7
25-29 Years	61	26.1	31	32.0		
30-34 Years	36	15.4	14	14.4		
Greater than 35 Years	20	8.5	9	9.3		
Maternal Height						
At or Below 1.67 meters	160	68.4	53	54.6	7.5	0.02
Between the 1.67 and 1.71 meters	38	16.2	28	28.9		
Above 1.71 meters	36	15.4	16	16.5		
Parity Status						
Nulliparous	96	41.0	38	39.2	0.1	0.9
Primiparous	73	31.2	31	32.0		
Multiparous	65	27.8	28	28.9		
Marital Status						
Married	54	23.1	32	33.0	3.7	0.2
Unmarried, Living with Baby's Father	91	38.9	31	32.0		
Unmarried	89	38.0	34	35.1		
Household Income						
Under US$25,000	175	74.8	65	67.0	2.1	0.1
US$25,000 or Higher	59	25.2	32	33.0		
Maternal Education						
Did not Finish High School	45	19.2	15	15.5	1.6	0.7
High School Graduate or GED	73	31.2	27	27.8		
Some College	77	32.9	35	36.1		
College Graduate or Higher	39	16.7	20	20.6		

Table 4. (cont'd)

Maternal Smoking Before/During Pregnancy						
Yes	66	28.2	36	37.1	2.6	0.1
No	168	71.8	61	62.9		
Gestational Diabetes[c] n= 330						
Yes	6	2.6	4	4.1	Fisher's Exact Test	0.6
No	227	97.0	93	95.9		
Gestational Hypertension[c] n= 330						
Yes	15	6.4	7	7.2	Fisher's Exact Test	0.9
No	218	93.2	90	92.8		

Abbreviations: ARCH, Archive for Research of Childhood Health; PA, physical activity; NHW, non-Hispanic/Latina White; NHB, non-Hispanic/Latina Black; BMI, body mass index; kg, kilogram; m, meter; diff, difference; var, variance.

[a] Birthweight z-score was calculated using the United States' gestational age and sex specific means and standard deviations. The sample's 70th percentile was calculated and used as the cut-point.

[b] Weight (kg)/height $(m)^2$

[c] Not included in covariates necessary for inclusion because they are mediators and were not intended to be used in model.

Table 5. Odds ratios for the odds of having birthweight z-score greater than the 70th percentile[a], ARCH Cohort 2010-2015.

Variable	OR	95% CI	
PA Category			
Sedentary	1.0	Referent	
Active, did not meet recommendations	1.3	0.7	2.4
Active, met recommendations	1.1	0.6	2.0
Maternal Height Category			
Less than or equal to 1.67 meters	1.0	Referent	
Between 1.67 and 1.71 meters	2.2	1.2	3.9
Above 1.71 meters	1.4	0.7	2.8
Maternal Race and Ethnicity			
NHW	1.0	Referent	
NHB	0.5	0.2	0.9
Other Race including Latina	0.8	0.4	1.6
Pre-Pregnancy BMI[b] Category			
Less than 25 kg/m^2	1.0	Referent	
25 - 29.9 vs Less than 25 kg/m^2	1.7	0.9	3.2
30 or greater vs Less than 25 kg/m^2	1.5	0.8	2.7
Maternal Smoking Before or During Pregnancy			
No	1.0	Referent	
Yes	1.5	0.9	2.5
Marital Status			
Married	1.0	Referent	
Unmarried	0.6	0.3	1.1
Unmarried, living with baby`s father	0.9	0.4	1.7

Abbreviations: ARCH, Archive for Research of Childhood Health; PA, physical activity; NHW, non-Hispanic/Latina White; NHB, non-Hispanic/Latina Black; BMI, body mass index; kg, kilogram; m, meter.

[a] Birthweight z-score was calculated using the United States' gestational age and sex specific means and standard deviations. The sample's 70th percentile was calculated and used as the cut-point.

[b] Weight (kg)/height $(m)^2$

Table 6. Summary of backward elimination [a], ARCH Cohort 2010-2015

Step	Effect Removed	DF	Number In	Wald Chi-Square	Pr > ChiSq
1	Education Level	3	9	0.22	0.97
2	Parity Category	2	8	0.53	0.77
3	Household Income	1	7	0.13	0.72
4	Maternal Age category	3	6	1.41	0.70

Abbreviations: ARCH, Archive for Research of Childhood Health; DF, degrees of freedom; Pr, Probability.
[a] To remain in model, variable had to have a p-value of less than 0.2.

Table 7. Association of predicted probabilities and observed responses of adjusted models, ARCH Cohort 2010-2015

Percent Concordant	65.4	**Somers' D**	0.31
Percent Discordant	34.3	**Gamma**	0.31
Percent Tied	0.3	**Tau-a**	0.13
Pairs	22698	**c**	0.66

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