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The Differential Effects of Prenatal Exercise Training Type on Maternal Glucose Metabolism: a Secondary Data Analysis of a Prospective Randomized Controlled Trial

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THE DIFFERENTIAL EFFECTS OF PRENATAL EXERCISE TRAINING TYPE ON MATERNAL GLUCOSE METABOLISM: A SECONDARY DATA ANALYSIS OF A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

STEPHANIE L. PROSTKO

44 Pages

Gestational diabetes mellitus (GDM) complicates 10-12% of pregnancies worldwide and poses significant, immediate, and long-term health risks to both the mom and baby. Importantly, consistent research demonstrates participating in sufficient levels of exercise during pregnancy may effectively manage maternal glucose levels, thereby potentially decreasing the risk of GDM. Most of these studies however, restricted their investigations to exposing pregnant women only to aerobic exercise. Previous studies in non-pregnant populations showed various exercise training types, such as resistance and combined (resistance + aerobic) training, elicited positive, independent effects on glucose metabolism, yet similar effects in pregnant women are unclear. PURPOSE: To evaluate differential effects of prenatal exercise training types during mid-to-late pregnancy on maternal glucose metabolism. METHODS: This study employed a secondary data analysis using data derived from a previously conducted, 24+ week prenatal exercise intervention. At 16 weeks of gestation, women were randomized to one of four groups: aerobic training (n= 89), resistance training (n= 61), combined training (n= 66), and non-exercising comparison group (n= 83). Exercise training groups participated in 3, 50-minute, moderate-intensity exercise sessions per week. The non-exercising group participated in 3, 50-minute, low-intensity stretching and breathing sessions per week. Maternal glucose metabolism was measured using fasting serum

glucose levels at 16, 25-27 and 36 weeks of gestation. GDM diagnoses were extracted from medical records and determined via oral glucose tolerance tests (OGTT) performed at prenatal clinics between 25-27 weeks of gestation. Three separate ANCOVA regression models were performed to evaluate the differential effects of prenatal exercise training type on maternal glucose metabolism at 25-27 weeks (using OGTT values), 36 weeks and the change from mid-to-late pregnancy (16-36 weeks). Maternal peak oxygen consumption and pre-pregnancy body mass index served as covariates. RESULTS: Prior to randomization into intervention groups baseline measures were taken from 299 women, including, age, pre-pregnancy body mass index (BMI), race and ethnicity, relative VO_2 max, and estimated 1 repetition maximum. Following baseline measures 299 women were randomized into the following: AT n= 89, RT n= 61, CT n= 66, and CON n= 83. An ITT analysis comparing the non-exercising control group at 25-27 weeks gestation, exercise training AT: 113.1 ± 3.4 mg/dL, 95% CI (106.4, 119.7), RT: 116.4 ± 5.3 mg/dL, 95% CI (105.9, 126.9), CT:113.3 ± 4.7 mg/dL, 95% CI (104.0, 122.6), CON: 115.2 ± 4.0 mg/dL, 95% CI (107.2, 123.2). Similarly, no between group differences in exercise training type were observed, AT vs. RT: -3.3 ± 6.3 mg/dL, 95% CI (-5.3,7.2), p= 1.0. AT vs CT: -0.3 ± 5.8 mg/dL, 95% CI (-6.0, 6.8), p=1.0, RT vs. CT: 3.1 ± 7.1 mg/dL, 95% CI (-7.3, 6.2), p= 1.0. Additionally, compared to the non-exercising control group at 36-weeks gestation, exercise training AT: 78.2 ± 1.5 mg/dL, 95% CI (75.1, 81.3), RT: 77.2 ± 1.7 mg/dL, 95% CI (73.7, 80.7), CT: 77.8 ± 1.8 mg/dL, 95% CI (76.1, 81.3), CON: 80.4 ± 2.2 mg/dL, 95% CI (76.1, 84.7). Likewise, no between group differences in exercise training type were observed, AT vs. RT: 1.0 ± 2.3 mg/dL, 95% CI (-7.7, 3.2), p= 1.0, AT vs. CT: 0.4 ± 2.4 mg/dL, 95% CI (-6.0, 6.8), p= 1.0 RT vs. CT: -6.0 ± 2.5 mg/dL, 95% CI (-7.3, 6.2), p= 1.0. Lastly, comparing the change in 16-week and 36-week glucose measures in the non-exercising control group, exercise training AT: -2.6 ± 1.8 mg/dL, 95% CI (-

6.2, 1.0) RT: -3.6 ± 2.0 mg/dL, 95% CI (-7.7, 0.4), CT: -4.7 ± 2.2 mg/dL, 95% CI (-9.0, -0.3), CON: 0.9 ± 2.6, 95% CI (-4.2, 5.9). No between group differences in exercise training type were observed AT vs RT: 1.0 ± 2.7 mg/dL, 95% CI (6.3, 8.4), p= 1.0, AT vs. CT: 2.1 ± 1.0 mg/dL, 95% CI (-5.6, 9.8), p= 1.0, RT vs CT: 1.0 ± 3.0 mg/dL, 95% CI (-7.0, 9.1), p= 1.0 between 16-week and 36-week glucose measures. These findings were consistent for both ITT and per-protocol analysis within the sample. CONCLUSIONS: This study demonstrates that AT, RT, and CT did not elicit appreciable effects on maternal glucose metabolism in mid and late pregnancy. Despite these statistically null differences, maternal glucose values showed lower values for all exercise training types compared to the non-exercising comparison group. Our sample consisted of metabolically healthy pregnant women (7% GDM prevalence) and small number of fasted glucose samples may have inhibited the discovery of detectable differences in maternal glucose metabolism between AT, RT, and CT in this study. Future studies should consider investigating the differential effects of exercise training type among metabolically-compromised women including those at-risk or a previous history of glucose intolerance.

KEYWORDS: GDM; Pregnant; Prenatal Exercise; Glucose; Exercise Training Type

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S.L.P.

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CHAPTER I: INTRODUCTION

Optimal maternal glucose metabolism is important for maintaining a healthy pregnancy as glucose is the primary substrate for optimal fetal growth and development[1]. In mid-to-late pregnancy, every pregnant woman exhibits increased peripheral insulin resistance, primarily at the skeletal muscle, inducing higher levels of circulating maternal glucose and subsequently, shunting the blood glucose to the fetus[15]. While this state of insulin resistance is natural during pregnancy, in some women it progressively worsens, resulting in the development of gestational diabetes mellitus (GDM)[1]. Over the past 15 years, the prevalence of GDM has increased in the US and worldwide, representing nearly 10% of all pregnancies[12, 24, 5]. GDM negatively affects the health of the mother and baby with increases in the risks of preterm birth, fetal/neonatal mortality, cesarean sections, future development of GDM and/or type 2 diabetes mellitus, infant macrosomia, altered fetal/neonatal metabolism and skeletal abnormalities[1]. Importantly, research demonstrates that chronic exercise exerts a potent effect on metabolism, potentially suggesting it as an effective solution for maintaining optimal maternal glucose metabolism.

Several studies conducted in the pregnant population indicate that chronic aerobic exercise during pregnancy[3, 11, 19, 22, 23]. In a 2018 systematic review and meta-analysis, Davenport et al., found that aerobic exercise training during pregnancy reduced the odds of GDM by 25%[11]. Additionally, reductions in circulating maternal capillary glucose and use of insulin therapy were observed[13, 19]. In support, well-established evidence shows enhanced peripheral glucose uptake, specifically in the skeletal muscle following exercise, which at rest accounts for nearly 80% of insulin-mediated glucose uptake[1, 19]. What remains unclear however, is whether the strong metabolic effect of chronic exercise exists across varying exercise training types. Nearly all prenatal exercise interventions exposed pregnant women to chronic aerobic exercise. While aerobic exercise is the most performed exercise during pregnancy and may positively affect maternal glucose metabolism, other exercise training types such as resistance exercise training and combined exercise training (aerobic plus resistance) are increasing in popularity and may elicit differential effects on maternal metabolism.

Previously studies conducted in non-pregnant populations showed that resistance only and combined exercise training types also positively affected glucose metabolism[4, 6, 7]. A 2018 systematic review concluded that among individuals with type 2 diabetes mellitus (T2DM), a metabolic condition similar to GDM, chronic resistance training improved glucose tolerance, insulin sensitivity, and increased skeletal muscle mass[10]. Importantly, some research suggests that various exercise training types may differentially affect glucose metabolism. Specifically, a randomized control trial assessing the independent effects of chronic aerobic, resistance, combined exercise training types in a sample of individuals with T2DM, found that the combined exercise training group elicited larger reductions in fasted serum glucose levels compared to the other exercise training groups[9]. Similar studies do not exist in the pregnant population. The few studies evaluating other exercise training types incorporated them in the same intervention group, thus precluding the assessment of their independent effects on maternal glucose metabolism[25,4,3]. Therefore, the independent effects of aerobic, resistance and combined exercise training on maternal glucose metabolism during pregnancy are unknown. What few studies have shown about exercise type training effect on maternal glucose metabolism is that aerobic, resistance, and combined exercise training could decrease the prevalence of GDM in pregnant populations[3, 5]. Specifically, aerobic only and resistance only exercise training has been shown to decrease need for insulin therapy[4]. Furthermore, combined exercise has been shown to decrease excessive weight gain during pregnancy[3]. Lastly, aerobic only exercise has shown an increase in glucose metabolism by eliciting a decrease in fasting blood glucose levels within exercise interventions[23,19,13].

The purpose of this study was to evaluate the effects of prenatal exercise type on maternal glucose metabolism, using data derived from a previously conducted 24+ week prenatal exercise intervention from mid-to-late pregnancy. We hypothesized that aerobic, resistance and/or combined exercise training would independently and differentially affect maternal glucose metabolism in mid-to-late pregnancy. Specifically, we posited that aerobic-, resistance-, and combined exercise-trained pregnant women would elicit lower levels of circulating serum glucose during their clinical oral glucose tolerance test (25-27 weeks of gestation), at 36 weeks of gestation and the change in glucose levels from 16 to 36 weeks of gestation compared to the non-exercise-trained pregnant women. Secondly, we hypothesized that combined exercise-trained and resistance exercise-trained pregnant women would exhibit the lowest and lower, yet healthy, levels of glucose and risk of GDM compared to aerobic exercise-trained pregnant women, respectively.

CHAPTER II: METHODS

Design

This study employed a secondary data analysis using data derived from a previously conducted 24+ week prospective randomized controlled exercise intervention trial in pregnant women (ENHANCED, 2015 - 2021). The ENHANCED by Mom study examined the effects of exercise training type (aerobic, resistance, combined) on several maternal, fetal, and neonatal health outcomes. At 16 weeks of gestation women were randomized to an aerobic, resistance, combined (aerobic + resistance) or stretching/breathing non-exercising control group and were followed until delivery (~40-41 weeks). Exercise groups performed 150 minutes of moderate-intensity exercise per week, while the stretching/breathing group participated in 150 minutes of stretching/breathing exercises per week. The primary outcomes of the ENHANCED by Mom study were fetal and neonatal cardiovascular function. Secondary outcomes of the parent study were maternal, fetal, and neonatal body composition, metabolism, pregnancy complications, and modes of delivery (e.g., vaginal, cesarean section). For the purposes of the *current* study, the outcomes of interest were maternal glucose metabolism in mid-to-late pregnancy, with serum glucose levels drawn at 16 and 36 weeks of gestation. Additionally, serum glucose values from routine prenatal oral glucose tolerance tests, occurring between 25-27 weeks of gestation, and subsequent GDM diagnoses were extracted from maternal medical records.

Sample

The ENHANCED by Mom study recruited a total of 373 participants between 2015 and 2021 in eastern North Carolina. Of these, 299 participants were deemed eligible and were randomized into one of four intervention groups: aerobic (n=89), resistance (n=61), combined (n=66) and stretching/breathing (n=83). Of the randomized participants randomized, 208 participants maintained ≥ 80% exercise adherence, yielding a per-protocol analytical sample, aerobic (n= 52), resistance (n= 45), combined (n= 50), and stretching/breathing (n= 61).

Recruitment

This ENHANCED by Mom study recruited pregnant women via brochures, fliers, social media (Facebook), word of mouth, local obstetric and gynecological offices, local businesses (gyms, daycares etc.), and university-wide email announcements. Pregnant women were eligible for this study if they, 1) were <16 weeks pregnant, 2) had a singleton pregnancy, 3) between the ages of 18 to 40 years of age, 4) had a body mass index (BMI) 18.50-34.99 kg/m^2, 5) able to participate in physical activity and not currently exhibiting any contraindications to exercise during pregnancy as outlined by the American College of Sports Medicine and American College of Obstetricians and Gynecologists, 6) were fluent in English, 7) had reliable transportation and, 8) did not use alcohol, tobacco and smokeless tobacco products, recreational or illicit drugs, or took medications affecting fetal growth. Pregnant women were excluded from this study if were currently diagnosed with any chronic conditions (e.g., hypertension, type 1 diabetes mellitus, type 2 diabetes mellitus). However, pregnant women who developed GDM continued their participation in the ENHANCED by Mom study.

All study protocols were approved by the East Carolina University and Vidant Medical Center Institutional Review Boards. The ENHANCED study is registered in ClinicalTrials.gov. Informed consent and physician clearance for physical activity were obtained prior to any study-related measurements or activities. Funding was obtained from the American Heart Association and internal Eastern Carolina University funds.

Metabolic Measures

Prior to randomization, participants underwent a submaximal exercise treadmill test following the modified Balke Protocol, previously established in pregnant women to indirectly estimate VO_{2peak}[19]. The modified Balke Protocol was used to determine maternal peak aerobic capacity and subsequently, determining individualized target HR zones for light (20 - 39% VO_{2peak}) and moderate (40 - 59% VO_{2peak}) intensities. Prior to the test, each participant was fitted with an indirect calorimeter requiring a nose clip and a breathing apparatus connected to a metabolic chamber. The indirect calorimeter measured oxygen consumption and carbon dioxide production, ventilation rate and respiratory exchange ratio. Additionally, the participant wore an electronic heart rate monitor (Polar FS2C), attached to an elastic chest strap at the level of the xiphoid process, which measured maternal heart rate continuously during the test. Next, the participant stood on the stationary treadmill for 3 minutes to measure “resting” oxygen consumption. Following, the exercise test commenced with a 5-minute warm-up where the participant walked at 3.0 mph at 0% grade. For the next 8 stages, the participant continued walking at a speed of 3.0 mph with 2% increments in grade every 2 minutes. For subsequent stages, walking speed increased 0.2 mph per 2 minutes at a constant 12% grade. The test was terminated if the 1) participant reached 85% of their age-predicted maximum heart rate ($220 - age_{years} \cdot 0.85$), 2) voluntary termination, 3) participant exhibited any of the ACOG contraindications to exercise during pregnancy. Upon termination of the test, participant performed a 5-minute the cool-down, walking at 1.5 - 2.0 mph at 0% grade. Maternal HR and blood pressure (via manual auscultation) are measured and recorded each minute and at the end of each stage, respectively. Rate of perceived exertion (RPE) using the Borg scale (6-20) was also measured every minute. RPE is a subjective measure of perceived exercise intensity, requiring the participant to consider their muscular fatigue, ventilation rate, HR etc., when providing their response. Ratings of 13 to 14 are considered moderate exertion, 15 is considered hard exertion, 17 and above is considered extremely hard or near maximal exertion. Oxygen consumption and carbon dioxide production was sampled in 30-second intervals. VO_{2peak} was defined as the greatest amount of oxygen consumed during the submaximal exercise test.

Muscular Strength

Following the modified Balke protocol, the strength capacity of the participants was measured via an estimated 1-repetition maximum (1RM) for most major and some minor muscle groups. Prior to each exercise, exercise specialists demonstrated proper technique to produce accurate estimations of strength and reduce the risk of injury. For each exercise, the participant performed, at maximum, three sets of 3 to 5 repetitions to estimate 1RM. Most exercises were performed on Cybex machines including leg press (quadriceps, gluteals, and hamstrings), leg extension (quadriceps), leg curl (hamstrings), shoulder press (front shoulder, anterior deltoid), chest press (pectoralis major), incline chest press (upper pectoralis major), triceps extension (triceps), latissimus dorsi pull down (latissimus dorsi), and seated row (trapezius, latissimus dorsi, teres group). Dumbbells were used to perform exercises primarily activating smaller muscle groups including bicep curls (biceps), lateral shoulder raises (deltoid group), and front shoulder raises (anterior deltoid).

Randomization

Following the aerobic and strength capacity tests, participants were randomized into one of the four groups, using a random sequence generator (GraphPad). Due to the nature of this study, the PI, exercise trainers and participants were not blinded to randomization, however the sonographer, cardiologist, magnetic resonance imaging technicians, and statisticians were blinded to group allocation.

Exercise Intervention

The ENHANCED by Mom study intervention employed a supervised, 24+ week prenatal exercise program including of four separate exercise training groups: aerobic, resistance, combine (aerobic plus resistance) and one non-exercising comparison group: stretching and breathing. All sessions were supervised, conducted on a one-on-one basis, lasted 50 minutes in duration and occurred 3 times per week on days and times that coincided with each participant's availability. At the beginning of each session, all groups performed an aerobic 5-minute warm-up that elicited a heart rate response between 20 – 30% of their $VO_{2\,peak}$. The intensity of each session was continuously monitored throughout each session using maternal heart rate (HR) via electronic Polar HR monitors worn on the chest at the level of the xiphoid process and Rating of Perceived Exertion (Borg Scale). Exercise sessions were designed to elicit a HR reflecting moderate intensity (40 - 59% $VO_{2\,peak}$) or a 12-14 rating on the Borg Scale. The stretching and breathing sessions were designed to elicit a HR reflecting light intensity ≤ 30% of $VO_{2\,peak}$ or ≤ 11 on the Borg Scale. Where needed, exercises and stretching positions were modified as pregnancy progressed to ensure safety and avoid discomfort during sessions. Prior to and following each session seated blood pressure via manual auscultation and HR were measured.

The ***aerobic only*** exercise training group performed 50 minutes of a self-selected aerobic exercise on one or more of the following machines: treadmills, ellipticals, stationary bicycles, and rowers. For any aerobic exercise, the participant self-selected the pace and resistance that elicited a HR in their moderate-intensity target HR zone for the duration of their exercise session.

The *resistance only* exercise training group sessions performed 8 to 10 resistive exercises for 2-3 sets of 10-15 repetitions each. Resistive exercise integrated multi-joint and single-joint exercises, targeting both large and small muscle groups of the lower and upper body regions. Resistive exercises were performed with Cybex machines, dumbbells, resistance bands, stability balls, exercise mats, and benches. Exercise intensity was primarily monitored through the Borg scale as previous research demonstrated HR is not an accurate measure of intensity during resistance exercise training. Resistance loads were initially prescribed at 50% - 60% of the participant's 1RM and modified to elicit a 12 and 14 on the Borg scale, corresponding to moderate intensity[19].

The *combined exercise* training group sessions performed 5, 10-minute circuits of aerobic and resistance exercise. Participants first performed 5 minutes of aerobic exercise on a machine of their choice at a self-selected pace and resistance that elicited a HR corresponding to their moderate-intensity heart rate threshold zone. Following, the participants performed 1 set of 4 to 5 resistive exercises for 10-15 repetitions. The resistance circuits incorporated multi-joint and single-joint exercises activating both large and small muscle groups of the upper and lower body regions. Resistive exercises were performed with Cybex machines, dumbbells, resistance bands, stability balls, exercise mats, and benches. During the resistive circuit, the Borg scale was used as the primary measure of exercise intensity. Resistance loads were initially prescribed at 50% - 60% of the participant's 1RM and modified to elicit a 12 and 14 on the Borg scale, corresponding to moderate intensity[19].

The *non-exercise control* group performed guided mindfulness, stretching, and breathing exercises for 50 minutes. For these exercises, women remained in seated, reclined, pronated or supinated positions. Stretches incorporated both large and small muscle groups and were paired with breathing techniques to promote body awareness. During these sessions, participants maintained a HR within their light intensity heart rate threshold zones and ≤11 on the Borg Scale.

Adherence to the exercise intervention was monitored via electronic attendance records. Pregnant women were considered "adherent" if they attended ≥ 80% of possible sessions during their prenatal period and received the prescribed dose of exercise.

Maternal Glucose Metabolism

Maternal glucose metabolism was expressed as fasted serum glucose levels at 16 and 36 weeks of gestation in addition to glucose values produced from their routine oral glucose tolerance test between 25 – 27 weeks of gestation and the subsequent GDM diagnosis. Serum glucose levels at 16 and 36 weeks were measured via fingerstick blood samples. All participants were instructed to perform an overnight fast (≥ 9 hours) drink adequate amounts of water prior to the blood draw. Fasted blood samples were collected between the hours of 6:00 am and 9:00 am to control for circadian rhythms. Fingerstick blood samples were collected by trained research staff, following established standard protocols. If an inadequate amount of blood was collected, a second fingerstick test was performed on the participant. Glucose values from the oral glucose tolerance tests administered in the participant's respective prenatal clinics and subsequent GDM diagnoses were extracted via maternal medical records.

Covariates

Several maternal demographic and pregnancy-related factors served as potential covariates including 1) age, 2) race/ethnicity, 3) peak aerobic capacity, 4) gestational weight gain, 5) parity, 6) gravida 7) pre-pregnant weight & height, and 7) infant sex. Information on maternal age, race/ethnicity, parity, gravida, pre-pregnancy weight and height were collected on the pre-screening eligibility questionnaire. Peak aerobic capacity was measured via a submaximal treadmill exercise test, previously described. Infant sex and delivery weight were extracted from medical records. Gestational weight gain was calculated via the difference in weight at delivery and prior to pregnancy. Maternal body mass index was calculated using self-reported pre-pregnancy height and weight and categorized as follows: normal weight (18.50-24.99 kg/m^2), overweight (25.00-29.99 kg/m^2), or obese class I (30.00-34.99 kg/m^2).

Statistical Analysis

Between-group differences in maternal demographic-, pregnancy- and exercise-related factors were determined via unadjusted ANCOVA regression models. Three separate ANCOVA regression models were performed in a stepwise manner to evaluate the effects of exercise training type on maternal glucose metabolism. Glucose metabolism was expressed as a continuous variable and represented 3 separate outcomes Model 1) mid-to-late pregnancy glucose metabolism – OGTT glucose concentrations at 25-27 weeks of gestation, Model 2) late pregnancy glucose metabolism glucose values at 36 weeks of gestation and Model 3) change in glucose metabolism from mid-to-late pregnancy – difference in glucose concentrations at 16 and 36 weeks of gestation. Because the prevalence of GDM was low in this sample (~7%), we were unable to robustly evaluate the effects of exercise training type on the risk of GDM in this study. All models were built similarly with the evaluation of the main effects followed by the sequential inclusion of select covariates. Covariates were included in the model if they meaningfully influenced the parameter estimates of the primary independent variable. Models 1, 2 & 3 included exercise training type (AT, RT, CT and CON), peak aerobic capacity expressed by ml.kg^{-1}.min and pre-pregnancy BMI expressed as kg.m^2. Model 3 additionally adjusted for maternal serum glucose at 16 weeks of gestation. Two separate analyses were performed, intention-to-treat (ITT) and per protocol (PP). ITT analyses included all subjects with complete data regardless of their adherence to their intervention group. PP analyses restricted the sample to ‘adherent’ pregnant women, defined as those attending $\geq$ 80% of possible exercise sessions and receiving the prescribed dose of exercise. Possible familywise error occurring with pairwise comparisons between exercise training types was accounted for using the Bonferroni correction factor. Adjusted β regression coefficients, standard errors and 95% confidence intervals (CI) were estimated using SPSS (IBM SPSS Statistics 26, Chicago Illinois). Statistical significance was set at $\alpha = 0.05$ for all analyses.

CHAPTER III: RESULTS

Baseline Characteristics

The sample consisted of 299 participants who were randomized into four exercise intervention groups: aerobic only training, resistance only training, combined training, and a stretching and mindfulness group (control). Thus, the final ITT analytical sample for the current study is 299, AT (n= 89), RT (n= 61), CT (n= 66) and CON (n= 83). The final PP analytical sample for the current study is 208, AT (n= 52), RT (n= 45), CT(n=50), and CON(n= 61). PP descriptive statistical analyses assessed descriptive characteristics and baseline measures for all four groups are listed in Table 2.

Table 1: PP- Maternal Demographic, Pregnancy, and Exercise-Related Factors by Intervention Group				
Maternal Characteristics	**AT (N=52)**	**RT (N=43)**	**CT (N=50)**	**CON (N=61)**
Demographic				
Age (yrs)	30.9 ±4.0	31.7 ±1.0	30.5 ±4.2	29.5 ±4.4
Pre-Pregnancy BMI $(kg{\cdot}(m^{-1})^2)$	24.5 ±4.6	25.0 ±4.2	25.7 ±4.4	26.7 ±6.1
% Overweight	23.1%	25.6%	34.0%	23.0%
%Obese	7.7%	11.6%	10.0%	18.0%
Race				
NH white	80.0%	81.4%	88.0%	70.5%
NH Black	9.6%	7.0%	6.0%	21.3%
Hispanic	1.9%	4.7%	4.0%	1.6%
Other	7.7%	7.0%	2.0%	3.3%
Pregnancy				
Parity	0.0 (0.0-3.0)	0.0 (0.0-3.0)	0.0 (0.0-2.0)	1.0 (0.0-3.0)
Gravida	2.0 (0.0-4.0)	2.0 (0.0-5.0)	1.0 (0.0-3.0)	2.0 (0.0-2.0)
16-week Glucose $(mg{\cdot}dL^{-1})$	80.1 ±7.5	80.1 ±5.9	81.4 ±8.7	80.6 ±6.9
36-week Glucose $(mg{\cdot}dL^{-1})$	78.4 ±7.6	77.1 ±8.2	78.7 ±7.0	81.5 ±14.4
OGTT $(mg{\cdot}dL^{-1})$	113.2 ±29.5	113.2 ±24.9	112.7 ±29.3	113.0 ±29.9
GDM (%Yes)	5.8%	9.3%	6.0%	8.2%
Gestational Weight Gain (lbs)	33.4 ±17.3	36.1 ±10.9	34.1 ±13.9	31.1 ±16.4
Infant Sex (%Male)	53.8%	53.5%	48.0%	45.9%
Exercise				
Relative $VO_{2\ peak}$ $(mL\ O_2{\cdot}kg^{-1}{\cdot}min^{-1})$	24.0 ±4.9	25.2 ±6.9	24.8 ±5.6	21.4 ±4.3
Weekly Exercise $(METmin{\cdot}week^{-1})$	724.0 ±229.5	576.7 ±134.1	652.4 ±195.6	338.0 ±148.1
Per-Protocol: Means (standard deviation), median (range) and proportions are reported, where appropriate. Overweight or obese categories were defined as follows: overweight (25.00-29.99 kg/m^2), or obese class I (30.00-34.99 kg/m^2). BMI = Body mass index. MET minutes per week were calculated by multiplying exercise intensity (METs = metabolic equivalent) x duration x frequency of sessions.				

Main Outcomes

ITT (all participants included regardless of exercise adherence) and PP (participants meeting or exceeding 80% exercise adherence) assessments analyzed glucose measures taken at 25-week and 27-week gestation. Covariates controlled for in the analyses were fitness level and pre-pregnancy BMI measures. All other covariates were excluded from analyses. There were no statistically significant findings in the ITT analysis comparing the control to the exercise groups at 25-weeks and 27-weeks of gestations (OGTT analysis): AT: β –2.1 ± 5.3 mg/dL, 95% CI (-12.6, 8.3), p= 0.7, RT: β 1.2 ± 6.7 mg/dL, 95% CI (-12.1, 14.1), p=0.9, CT: β -1.9 ± 6.2 mg/dL, 95% CI (-14.3, 10.4), p= 0.8. There were no statistically significant differences between exercise groups at 25 to 27-weeks gestation, AT vs RT: -3.3 ± 6.3 mg/dL, 95% CI (-5.3, 7.2), p=1.0, AT vs. CT: -0.3 ± 5.8 mg/dL, 95% CI (-6.0, 6.8), p=1.0, CT vs. RT: 3.1 ± 7.1 mg/dL, 95% CI (-7.3, 6.2), p=1.0. There were no statistically significant findings in the PP analysis glucose measures between the control group and the exercise groups: AT: β -0.3 ± 3.4 mg/dL, 95% CI (-7.1, 6.4), p=0.9, RT: β -3.3 ± 3.5 mg/dL, 95% CI (-10.2, 3.7), p=0.4, CT: β -1.6 ± 3.4 mg/L, 95% CI (-8.4, 5.1), p=0.6. Likewise there were no statically significant differences between exercise groups: AT vs. RT: -2.4 ± 7.7 mg/dL, 95% CI (-23.1, 18.2), p=1.0, AT vs. CT: -0.6 ± 7.2, 95% CI (-19.9, 18.6), p=1.0, RT vs. CT: 1.8 ± 8.3 mg/dL, 95% CI (-20.6, 24.2), p=1.0.

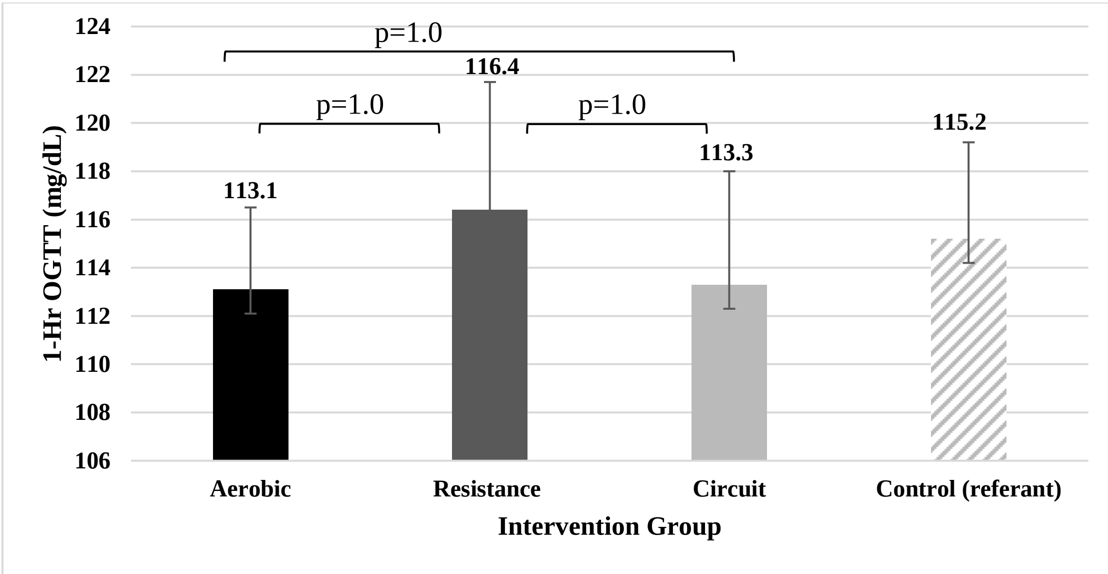

Figure 1.1 ITT: Maternal Oral Glucose Tolerance Test Values in Mid-Pregnancy, by Group: Maternal oral glucose tolerance test values in mid-pregnancy were extracted from medical records.

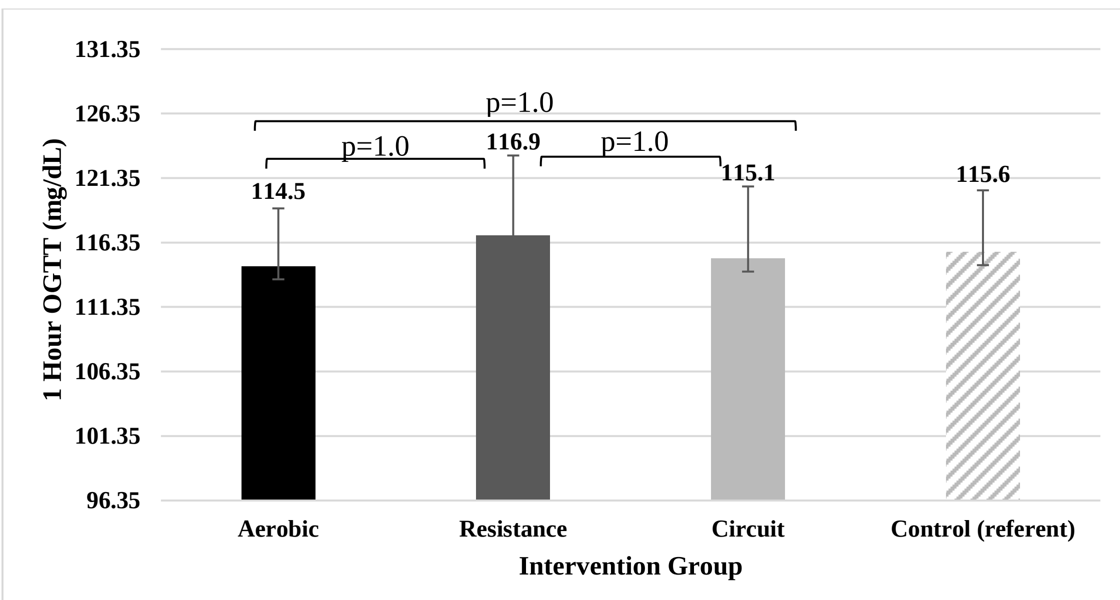

Figure 1.2 Per-Protocol: Maternal Oral Glucose Tolerance Test Values in Mid-Pregnancy, by Group**:** Glucose value**s** were extracted from medical records.

There were no statistically significant differences in the ITT analysis comparing the exercise group 36 week measures to each the non-exercising group: AT: β -2.2 ± 2.7 mg/dL, 95% CI (-7.7, 3.2), p= 0.4, RT: β: -3.2 ± 2.8 mg/dL, 95% CI (-8.8, 2.5), p=0.3, CT: β -2.6 ± 2.9 mg/dL, 95% CI (-8.1, 2.9), p=0.4. Likewise, there were no statistically significant differences found in the in-between group mean differences, AT vs. RT: 1.0 ± 2.3 mg/dL, 95% CI (-5.3, 7.2), p=1.0, AT vs. CT: 0.4 ± 2.4 mg/dL, 95% CI (-6.0, 6.8), p=1.0, RT vs. CT: -0.6 ± 2.5 mg/dL, 95% CI (-7.3, 6.2), p=1.0. Furthermore, there were no statistically significant differences in the PP 36-week glucose analysis when comparing the exercise groups to the control, AT: β -0.3 ± 3.4 mg/dL, 95% CI (-7.1, 6.4), p=0.9, RT: β -3.3 ± 3.5 mg/dL, 95% CI (-10.2, 3.7), p= 0.4, CT: β -1.6 ± 3.4, 95% CI (-8.4, 5.1), p= 0.6. Similarly, there were no statistically significant differences found in between exercise group comparisons, AT vs. RT: 2.6 ± 2.7 mg/dL, 95% CI (-4.4, 10.3), p=1.0, AT vs. CT: 1.3 ± 2.7 mg/dL, 95% CI (-5.9, 8.5), p=1.0, RT vs. CT: -1.6 ± 2.8 mg/dL, 95% CI (-9.1, 5.8), p=1.0.

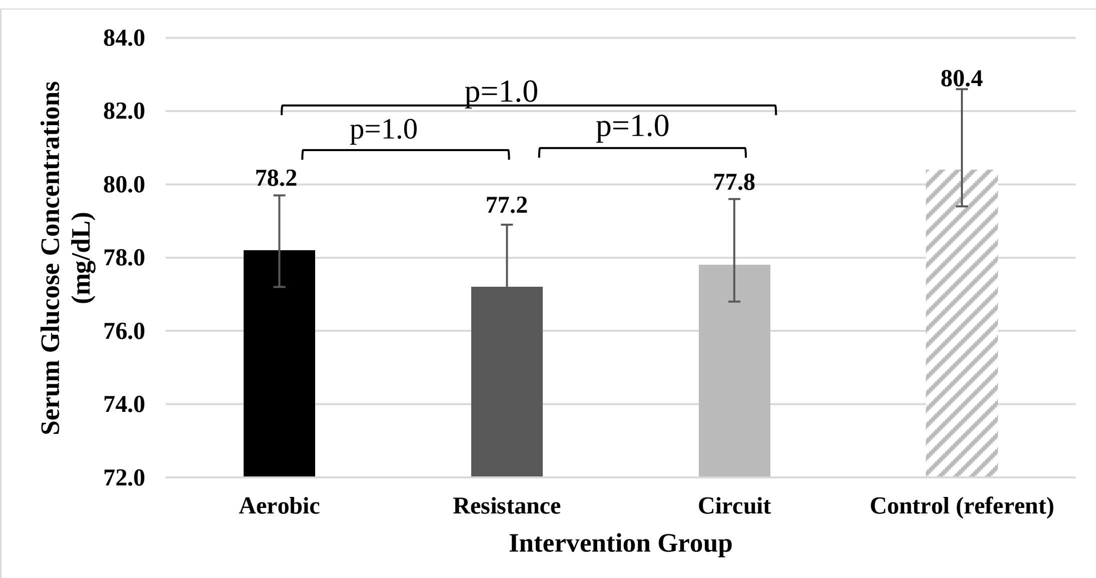

Figure 2.1 ITT: Maternal Serum Glucose Levels at 36 weeks of Gestation, by Group: Maternal serum glucose levels were measured at 36 weeks of gestation via fingerstick.

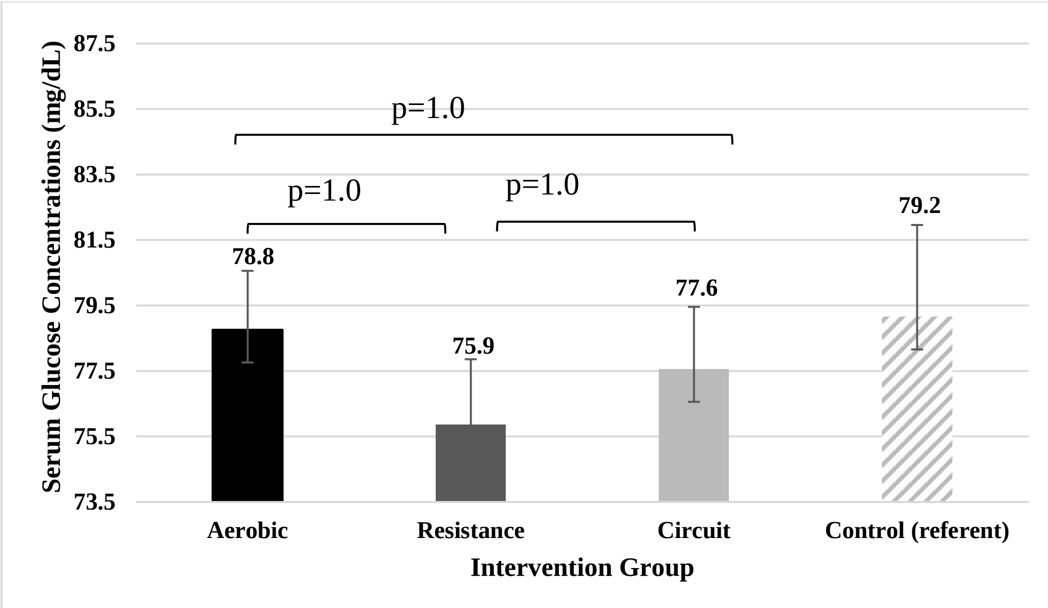

Figure 2.2 Per-Protocol: Maternal Serum Glucose Levels at 36 weeks of Gestation, by Group. Glucose measures were collected via fingerstick.

There were no statistically significant differences found in the ITT analysis assessing change in 16-week and 36 -week glucose measures between the non-exercising control group and the exercising groups: AT: β -3.4 ± 23.2 mg/dL, 95% CI (-9.7, 2.8), p=0.3, RT: β -4.5 ± 3.3 mg/dL, 95% CI (-11.1, 2.1), p= 0.2, CT: β -5.5 ± 3.3 mg/dL, 95% CI (-12.1, 1.0), p= 0.1. Likewise there were no statistically significant findings found in between exercise groups, AT vs. RT: 1.0 ± 2.7 mg/dL, 95% CI (6.3, 8.4), p=1.0, AT vs. CT: 2.1 ± 2.9 mg/dL, 95% CI (-5.6, 9.8), p=1.0, RT vs. CT 1.0 ± 3.0 mg/dL, 95% CI (-7.0, 9.1) p= 1.0. Additionally, there were no statistically significant differences found in the PP analysis assessing change in 16-week and 36-week glucose measures between the non-exercising control group and the exercising groups: AT: β -1.0 ± 2.8 mg/dL, 95% CI (-6.6, 4.6), p=0.7, RT: β -6.3 ± 4.1 mg/dL, 95% CI (-14.4, 1.8), p= 0.1, CT: β -5.3 ± 4.0 mg/dL, 95% CI (-13.4, 2.7), p= 0.2. Furthermore, there were no statistically significant findings found in between exercise groups, AT vs. RT: 4.0 ± 3.2 mg/dL, 95% CI (-

4.5, 12.7), p= 1.0, AT vs. CT: 3.1 ± 3.2 mg/dL, 95% (-5.6, 11.7) p= 1.0, RT vs. CT: -1.0 ± 3.3 mg/dL, 95% CI (-9.9, 8.0), p=1.0.

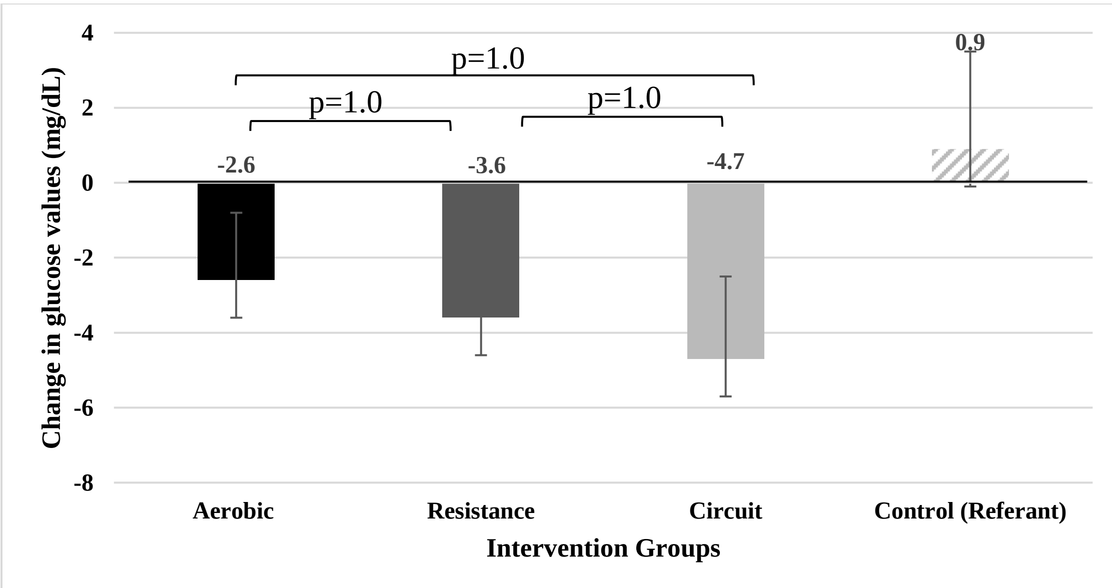

Figure 3.1 ITT: Change in Maternal Serum Glucose from Mid-to-Late Pregnancy, by Group: Shows the change in maternal serum glucose measured via fingerstick at weeks 16 and 36 of gestation.

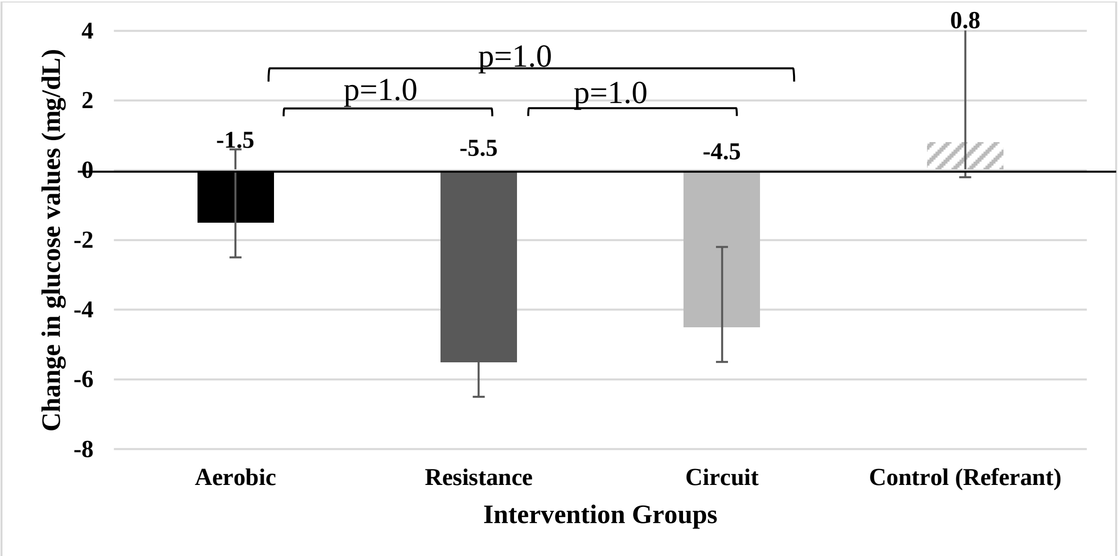

Figure 3.2 Per-Protocol: Change in Maternal Serum Glucose from Mid-to-Late Pregnancy, by Group: Shows the change maternal glucose concentrations from 16 to 36 weeks of gestation by group.

Supplementary Outcomes

An ANCOVA regression analysis assessing the influence of fitness level on maternal glucose found fitness and BMI influenced glucose as depicted by supplementary Tables 3 and 4 found in Appendix B. All multiple linear regression models controlled for familywise error according to the Bonferroni method when measuring in-between group differences among the exercise groups.

CHAPTER IV: DISCUSSION

The main purpose of this study was to evaluate differential effects of prenatal exercise training types on maternal glucose levels in mid-to-late pregnancy. We hypothesized that both resistance and combined exercise trained pregnant women would elicit lower levels of serum glucose in mid-to-late pregnancy, with the combined exercise trained group exhibiting the lowest concentrations. The major findings of this study were 1) compared to the non-exercising comparison group, AT, RT, nor CT affected maternal glucose metabolism at any measured timepoint and 2) AT, RT and CT did not elicit differential effects on maternal metabolism at any measured timepoint.

Unexpectedly, this study observed no between-group differences in exercise training type on maternal glucose metabolism from mid-to-late pregnancy. Given the strong metabolic effects of both aerobic and resistance exercise found in non-pregnant and some pregnant populations, we anticipated lower glucose values among all exercise training types compared to the non-exercising comparison group, at minimum, and possibly the lowest glucose values among the exercise groups incorporating resistive exercises. Considering our population consisted of women who were healthy weight as well as overweight and obese, it is possible that the results are diluted to the fairly healthy population of women enrolled. Furthermore regarding the null effects of exercise training type on the glucose values derived from the OGTT test during 25-27 weeks of gestation, it is possible that the 9 to 11-week training period (16 weeks of gestation until the OGTT) was insufficient to yield appreciable metabolic adaptations consequent to exercise training, especially considering the healthy population of women. Adaptations to exercise range according to the population studied and the type of exercise performed. A systematic review looking at metabolic adaptations to exercise in endurance and strength training protocols in a non-pregnant population saw adaptations occurring between 8 to 12 weeks of exercising[16]. A systematic review assessing maternal metabolic adaptations to aerobic exercise found improvements in cardiovascular fitness as early at 19 weeks into the intervention[22]. There is sparse research that has assessed how quickly maternal metabolism adapts to exercise interventions. Therefore, it could be possible that the sample in the EHNANCED study did not have enough training time between glucose measures to elicit metabolic adaptations to the exercise programming. Interestingly however, non-statistically significant differences in the magnitude of OGTT glucose values were observed, with the adherent aerobic and combined exercise trained group eliciting the lowest glucose values. Our null observations contrast with other studies evaluating the effects of aerobic and/or combined exercise training on maternal glucose metabolism measured via OGTT. A study conducted in 2018 employing a randomized controlled trial exposing pregnant women to aerobic exercise (EG), found statistically significant differences in OGTT values comparing the EG group to the non-exercising control group (CG), EG: 116.6 mg/dL vs. CG: 121.6 mg/dL, U=23, 158, p= 0.045, specifically lower values among the exercise-trained pregnant women.[3] The protocol of the 2018 exercise intervention was similar to this study where participants met 3 times a week for 55-60 minute supervised sessions whereas the ENHANCED exercise protocol met 3 times a week for 50 minute supervised sessions. However, it could be possible that the 2018 study found statistically significant OGTT outcomes between groups due to larger sample size and the control protocol. The control group received nutritional and exercise education from doctors but did not perform any form of supervised exercise activity. It is possible that majority of the control group did not exercise. In the ENHANCED study, the control group performed mindfulness and breathing exercising which, depending on maternal fitness level, could have elicited a light intensity heart rate response impacting maternal glucose levels, potentially explaining the contrast in our findings versus the literature. Light intensity exercise has been shown to decrease maternal glucose levels[20]. Furthermore, a different study employing a 12-week, prenatal combined aerobic and resistance exercise intervention meeting once a week in 2012, found statical significance in between group OGTT measures, (Exercise vs. Control: -0.13 mmol/L). Besides the difference exercise protocols between the ENHANCED study and the 2012 study, it could be possible that statical significance was found in OGTT measures due to the difference in sample sizes, ENHANCED sample, n= 299, 2012 study sample, n=702[2].

Our study also did not observe significant differences between exercise training types and maternal glucose metabolism in late pregnancy (36 weeks gestation) nor throughout mid-to-late pregnancy (16 to 36 weeks of gestation). Interestingly however, albeit non-significant, lower glucose values at 36 weeks of gestation and smaller increases in the changes in glucose from 16 to 36 weeks were observed among the exercise training groups. Moreover, the resistance and combined exercise-training groups appeared to exhibit the lowest glucose values at these timepoints. Most likely the lack of significant findings is related to the healthy population, which includes healthy women across BMIs. Further research is needed to focus on a less healthy population and/or the obese women only. Further, due to the healthy sample in our study, average glucose values were normal across all four groups at the three glucose measures assessed in the intervention, 16-week, 25-27- week (OGTT), and 36-weeks. Within this sample, there was only a 7% prevalence of GDM. This prevalence is lower than the current worldwide prevalence of 10.6%[5]. Non statically significant findings were also found in a 2010 randomized control trial employing a resistance training exercise intervention. The sample being evaluated in this study were pregnant women diagnosed with GDM and requiring insulin supplementation. Participants were randomized into either an exercise and insulin group and insulin only group. Although no findings were significant, the 2010 study observed a decrease in the need for insulin supplementation and lower blood glucose levels in the exercise and insulin group versus the insulin only group[4]. These findings are similar to the outcomes of this current study however, statistical significance was probably diluted in the 2010 study due to the use of insulin in both groups. However, this does imply that resistance training could have some effect on maternal glucose metabolism.

In a study analyzing the effect aerobic exercise has on glucose metabolism in 2020 found significant 36-week glucose measures between the aerobic exercise and control group. The aerobic exercise group decreased glucose measures at 36-weeks compared to the control group[19]. Our findings do not align with the glucose findings in the 2020 study potentially because the 2020 study control group may have been a true non-exercising control. As mentioned above the ENHANCED study control group elicited a light intensity heart rate response. Furthermore, the difference in sample sizes between groups, the 2020 study had more participants in the control than the aerobic group versus the ENHANCED study had more participants in the aerobic group than the control. Having more individuals in the control group could strengthen statistical significance because more people are not exercising potentially leading to an increase in glucose because any excess would not be utilized through exercise.

Other potential explanations for our null findings include the tight regulation of glucose during pregnancy, unmeasured biomarkers, and exercise programmatic differences. Glucose serves as the primary fuel source for optimal fetal growth and development. Several changes in maternal physiology occur during pregnancy such as increased hormone production and concentrations (e.g., human placental lactogen, cortisol, estrogen, progesterone, and prolactin), peripheral insulin resistance, hypertriglyceridemia etc., all of which contribute to the dramatic metabolic shift in mid-to-late pregnancy that shunts a majority of maternal glucose to the fetoplacental unit[20]. Thus, we speculate that severe perturbations to maternal glucose metabolism such as glucose intolerance, previous history of GDM or current diagnosis of T2DM, maybe required to alter the tight regulation of maternal glucose and for exercise to exert a positive effect. In support of this, our study observed that among women diagnosed with GDM, all exercise training types elicited lower OGTT values, with pregnant women in the resistance exercise group exhibited the lowest OGTT values, AT: 155.5 ± 23.0 mg/dL, RT: 115.0 ± 29.7 mg/dL, CT: 147.5 ± 14.8 mg/dL, CON: 167.3 ± 29.7 mg/dL. It is important to note that the sample size (AT: n=6, RT: n=2, CT: n=0 CON: n= 4) that showed this response was incredibly small and had no statical significance in the main analysis. It is possible that while glucose remained unaffected by exercise, that other biomarkers associated with its metabolism were affected, but not measured in this study. For example, in another study analyzing the ENHANCED by Mom pregnancy cohort, the authors found lower levels of circulating insulin at 36 weeks of gestation in aerobic exercise-trained pregnant women compared to the non-exercising pregnant women[20]. Those findings may suggest improved glucose metabolism consequent to chronic aerobic exercise.

Lastly, it is possible that statistically significant lower glucose values were not observed, specifically among the resistance and combined exercise training group as hypothesized, were due to the focus of the resistance training aspect of the exercise program. The sets and repetitions scheme prescribed reflective a muscular endurance training focus. With this focus, lean body mass gains are minimal (at least in non-pregnant populations) consequently minimizing the potential metabolic effect of resistance exercise training. Rather, hypertrophy-focused programs which elicit larger gains in skeletal muscle mass, may more effectively impact maternal glucose metabolism. No studies to date have evaluated the metabolic effects of various resistance training programs during pregnancy.

Strengths & Limitations

This study possesses both strengths and limitations warranting attention. The greatest strengths of this study lie in its rigorous study design (randomized controlled trial), the inclusion of 3 distinct exercise training groups allowing for the evaluation of the independent effects of different exercise training types, a first of its kind and the supervised exercise training sessions. The primary limitations of this study include the metabolically healthy sample of pregnant women. Only 7% the sample presented with GDM and only two participants had a previous history of GDM. Moreover, the average glucose values at all measurement timepoints fell within normal, healthy ranges. Consequently, the healthy levels of glucose metabolism likely decreased the potential metabolic effect of exercise training type. A second limitation of the study was the small number of fasted glucose samples at 16 and 36 weeks of gestation and its comparison across 4 intervention groups, this likely reduced statistical power. A third limitation was the non-exercising comparison group. The mindfulness, breathing, and stretching exercises were performed light intensity efforts, possibly reducing the differences in glucose metabolism. Other studies showed that light intensity exercise may impact physiological biomarkers, while not to the extent of higher intensities, but enough to minimize the differences between the groups and precluding the detection of a significant difference in glucose metabolism.[3]

In future analysis recruiting pregnant women early in pregnancy and women with maternal glucose intolerance, T2DM, or history of GDM should be included in future samples. Secondly, the addition of more glucose measures throughout the intervention would allow for trajectory glucose values to be shown as the mother's body adapted to exercise. Lastly, a change in the programming of the resistance training group from endurance to hypertrophy formatting may elicit a noticeable change in blood glucose levels.

Despite the lack of significant values found in this study, there was a small observation of glucose levels between exercise groups and the control groups for all three glucose measures. Given the lack of significance between group measures, this study suggests that there could be an influence of exercise on maternal glucose metabolism. Future research must be conducted to assess the influence of various exercise type on maternal glucose metabolism, especially in a less healthy population. The hope of this study was to inform clinicians and expecting mothers which exercise type was the most efficient and effective in managing maternal blood glucose to promote a healthy pregnancy.

CHAPTER V: EXTENDED LITERATURE REVIEW

This literature review analyzes the current state of the scientific evidence examining the influence of exercise training types on maternal glucose metabolism and the risk of gestational diabetes mellitus (GDM). Specifically, this section reviews the following topics1) maternal glucose metabolism -maternal and fetal adverse health consequences, 2) the effect of exercise on glucose and development of type 2 diabetes mellitus, and 3) the impact of exercise on glucose metabolism during pregnancy.

Maternal Glucose Metabolism

Skeletal muscle mass (SKM) is a large tissue bed, accounting for nearly 40% of body mass and 80% of insulin-mediated glucose uptake, suggesting its potential for a potent metabolic effect. For SKM to elicit its metabolic effect, it must be activated via exercise at a sufficient dose. SKM activation depletes glycogen stores during exercise leading to the translocation of glucose transmitter type 4 (GLUT4) to the cell surface to retrieve glucose[8]. Glucose uptake is stimulated by skeletal muscle contraction. Skeletal muscle contraction occurs to some extent in all forms of exercise. As the exercise becomes habitual metabolic changes occur in skeletal muscle to increase insulin sensitivity. An increase of insulin receptors simultaneously increases the GLUT4 which allows glucose to be taken in by the cell through facilitated diffusion. Resistance exercise specifically increases GLUT4 concentration and rate of metabolism[8]. Therefore, exercise can be used as a non-pharmacological intervention in the management of glucose metabolism. This information could be useful for all individuals that have a form of diabetes, such as type 2 diabetes mellitus (T2DM) or gestational diabetes mellitus (GDM).

There are numerous metabolic changes that occur during a normal pregnancy, which include a change in glucose metabolism and tolerance. In order to provide glucose to the fetus for growth and development, the body develops a diabetogenic environment where the mother's blood levels express high levels of blood glucose and insulin. This environment is created by a decrease in insulin sensitivity and skeletal muscle uptake in the mother's cells[15]. As the mother's body adapts glucose levels may become too high or too low. An excess of blood glucose blood levels is more common than insufficient blood glucose levels. Roughly 10% of pregnancies have high blood glucose levels that develop into a metabolic syndrome known as gestational diabetes mellitus (GDM). GDM is defined as glucose intolerance that occurs during pregnancy and usually develops later in pregnancy[1]. All pregnant women undergo venipuncture blood glucose screenings to measure fasting blood glucose and insulin levels at during mid-to-late pregnancy. This screening will determine if a mother has developed glucose intolerance or GDM[1]. In obese individuals, GDM tends to develop earlier in pregnancy however, the women that are at the highest risk of developing GDM are those who have uncontrolled type 2 diabetes mellitus prior to pregnancy[15]. Other individuals who are at higher risk of developing GDM include individuals with high pre-pregnancy BMI and Asian/Pacific Islanders and Hispanics.

Health Consequences of Poor Glucose Metabolism

Both the women and the fetus are affected during gestation and post-pregnancy by GDM. Mothers have a higher risk of developing T2DM after pregnancy or developing GDM in their next pregnancy. GDM has the potential to cause dysfunction in the placenta, preterm birth, defects in fetal neural tubes, increase risk in cardiometabolic disease, and produce excessively large birth weights[1]. Additional risks that GDM has on the fetus include skeletal abnormalities, a slight decrease in brain size, predisposition to developing a form of diabetes, increased adipocytes, and premature maturation of pancreatic beta cells resulting in poor insulin management[14]. Mothers that develop GDM during pregnancy are at higher risk of delivering preterm or losing the baby than in normal pregnancy[21].

If a woman has a confirmed diagnosis of GDM it is important to start a treatment intervention immediately for a healthy pregnancy and delivery. Women may choose a pharmacological treatment, non-pharmacological treatment, or both to control the metabolic disease[1]. Non-pharmacological treatment involves behavioral changes such as diet and exercise. Exercise has been shown to improve glucose metabolism in individuals with T2DM.

Prenatal Exercise as a Solution

Aerobic Exercise

Aerobic training is defined as performing exercises that rhythmically and continuously move large muscle groups for sustained periods of time such as walking, cycling, rowing, swimming, running, etc.[1]. Aerobic training focuses on improving cardiorespiratory fitness.

Aerobic exercise has shown to be a positive treatment for diabetes if not limited by comorbidities[10]. Previous research has shown that performing aerobic exercise within the first 20 weeks of pregnancy decreases a woman's risk of developing GDM by managing maternal glucose levels

Resistance Exercise

Resistance training is defined as a form of exercise characterized by repetitive voluntary skeletal muscle contractions working against an external resistance (e.g., gravity during bodyweight exercises, free weights) and is designed to improve muscular fitness[1]. Resistance training focuses on improving muscular strength. There are different forms of resistance training which include strength training and circuit training. Strength training involves heavier weights, lower repetitions, increased recovery time between sets and isolates muscle groups[1]. Circuit training involves full-body exercises performed in a specific order with minimal rest between exercises[1].

Anaerobic exercise training, resistance training, stimulates glucose metabolism and is still being researched to be safe and effective to manage diabetes[10]. Pregnant women tend to avoid resistance training due to misconceptions that resistance training will harm the fetus, harm the mom, or increase gestational discomfort[1]. Given the lack of research on resistance training's effect on the development of GDM, most women are recommended to perform aerobic exercise as a therapeutic intervention.

Combined Exercise

Combined exercise training is defined as a pairing of resistance and aerobic training. Combined exercise training improves cardiovascular and muscular health. A combined exercise session would include strength-building exercises and cardiovascular exercises performed in a circuit style[1].

Aerobic Exercise Training and GDM

Studies assessing the relationship between maternal glucose metabolism and exercise commonly involve an aerobic exercise intervention. A randomized control trial performed in 2016 analyzed the effectiveness of a 12-week aerobic exercise intervention on glucose metabolism. Participants met 3x a week to perform aerobic exercise sessions. The researchers found when comparing pre-intervention fasting blood glucose levels to post-intervention fasting blood glucose levels that there was a decrease in fasted glucose levels. These results suggest that glucose levels have the ability to decrease when performing aerobic exercise for 12 weeks in a pregnant population[13].

In 2020 a secondary data analysis assessing a 24+ week aerobic-only exercise intervention in pregnant women and its effect on exercise found a decrease in insulin levels and need for insulin therapy late in pregnancy. These findings suggest that performing 150 minutes of moderate-intensity exercise during the week could lower insulin levels and decrease the need for insulin therapy late in pregnancy[19]. A systematic analysis conducted in 2018 reviewed the relationship on aerobic exercise and GDM prevention. After reviewing 106 studies assessing randomized controlled trials involving exercise-only interventions the researchers found that performing roughly 140 minutes of aerobic exercise had the ability to reduce the risk of GDM by 25%[11].

Exercise Type & Glucose Metabolism in T2DM

Type 2 diabetes mellitus is defined as a group of metabolism alterations that lead to a decrease in insulin sensitivity in peripheral tissues contributing to an inability to regulate blood glucose levels within the body[10]. It is considered a chronic-degenerative metabolic disease that is initially characterized by high blood glucose and blood insulin levels.

In 2011 a randomized control trial assessed different types of exercise and their effects on glucose metabolism in individuals with T2DM. The exercise intervention randomized participants into four groups: aerobic only, resistance only, combined resistance and aerobic, and control. Participants completed three weekly exercise protocols according to their assigned groups for nine months. The researchers sampled hemoglobin (HbA1c) pre and post-intervention via fingerstick. The HbA1c results showed that the combined exercise group produced larger decreases in blood levels compared to the smaller decreases produced by the aerobic only and resistance only exercise groups in post-intervention measures. The control group had little to no change in HbA1c levels. The results suggest that performing combined exercise three times a week for 9 months could lower HbA1c[9].

A systematic review conducted in 2018 evaluated randomized controlled trials that analyzed the relationship between resistance training and glucose metabolism in a T2DM population. The researchers found that resistance training exercise interventions improved glucose tolerance, increased insulin sensitivity, and increased muscle mass. These findings suggest that performing resistance training on a weekly basis could lead to improved glucose tolerance and insulin sensitivity in individuals with T2DM[10.]

The research that has been conducted involving various forms of exercise and T2DM indicates that exercise is an effective way to manage glucose metabolism in non-pregnant populations. Aerobic exercise is typically recommended for T2DM glucose management however, glucose uptake is stimulated by the contraction of skeletal muscle. Individuals with T2DM can choose their preferred exercise training, resistance, aerobic, or combined and still improve glucose metabolism. Research has found that resistance training is becoming more popular among T2DM as it is easier to perform longer exercise sessions in comparison to aerobic training sessions. The longer the training session the more glucose will be metabolized[1]. In some research resistance training has shown better improvements in glucose metabolism which assumes that more muscle contractions are occurring during resistance exercise sessions than aerobic exercise. These findings in a non-pregnant population that has poor glucose metabolism could be promising for a pregnant population who has poor glucose metabolism.

The Effects of Exercise on Maternal Glucose Metabolism

There is very little research that evaluates the effects of resistance and combined exercise training on glucose metabolism and the risk of developing GDM. Many studies analyzing the relationship between maternal glucose metabolism and exercise involve aerobic exercise training. A systematic review evaluated different exercise interventions assessing the independent effects of various types of exercise in a pregnant population. Researchers found that there were less resistance and combined exercise interventions than aerobic exercise interventions. The exercise intervention studies involving aerobic exercise training in a pregnant population have shown to have a positive impact on glucose metabolism. In the few studies analyzing combined resistance and aerobic training, it was found that combined training increased muscular strength. There were not enough resistance training exercise interventions to collect enough evidence on the effect on maternal glucose metabolism[22].

When a woman is diagnosed with GDM and fails to adopt a change in diet and an increase in exercise the next form of therapy recommended is insulin therapy to manage glucose metabolism. In a study observing the effects of an elastic band resistance exercise program paired with insulin therapy compared to insulin-only therapy in women with GDM, it was found that women required less insulin supplementation in the exercise group than those who did not exercise[4]. In the elastic band resistance exercise program paired with insulin therapy, some women were able to discontinue the insulin therapy and continue to manage glucose metabolism through exercise only.

Another study analyzed the effects of resistance training exercise paired with a diabetic diet and a diet-only approach in managing glucose metabolism in women with GDM. In this study individuals who performed a resistance training exercise and followed a diabetic diet delayed the need for insulin therapy longer than women who followed only a diabetic diet. These results were the same in individuals that had both high and normal BMI's during gestation[7]. When pairing resistance training and a diabetic diet together women were prescribed smaller amounts of insulin than women who did not exercise[7]. Regardless of insulin supplementation or noninsulin supplementation women who perform exercise, either aerobic or resistance, have been shown to maintain healthy blood glucose levels for longer periods of time than women who do not exercise[4].

In 2018 a randomized controlled trial was performed to assess the effects of combined exercise on the prevalence of GDM and maternal weight gain. Participants performed combined exercise for 8-10 weeks on a weekly basis. When comparing pre-intervention to post-intervention measures the researchers found a decrease in the prevalence of GDM and in excessive weight gain in the combined exercise group compared to the control. These findings suggest that combined exercise performed for 8-10 weeks could elicit a positive effect on minimizing excessive weight gain and decreasing the prevalence of GDM[3].

Conclusion

As mentioned previously there are few studies that assess the effects of various types of exercise on maternal glucose metabolism and the risk of GDM. Most of the studies that do assess the relationship of exercise and maternal glucose metabolism usually involve aerobic only exercise. There are some exercise interventions that assess combined exercise interventions and the effect of exercise on maternal glucose metabolism, but few studies assess, aerobic only, resistance only, and combined exercise side by side. Furthermore, randomized controlled trials assessing the effect resistance training has on maternal glucose metabolism oftentimes include light intensity workouts and use equipment that challenges the ability to progressively overload participants throughout the progression of the intervention. Lastly, the independent effects of various exercise types remain unknown in the current literature. Knowing what type of exercise elicits the best maternal glucose metabolism will help maintain a healthy pregnancy for pregnant women and provide health care professionals with a more specific form of glucose management behavioral therapy.

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APPENDIX A: PRE-PROTOCOL FORMS

1-RM Strength Testing				
Exercise	T-1 Weight	T-2 Weight	T-3 Weight	Final Weight
Leg Press				
Chest Press				
Seated Row				
Leg Extension				
Shoulder Press				
Lat Pull Down				
Leg Curl				
Tricep Extension				
Incline Chest Press				
DB Bicep Curl				
DB Lateral Shoulder				
DB Front Shoulder				

Table 2: 1-RM Strength Test Protocol Sheet

Modified Balke Treadmill Test Protocol (VO_{2peak} pre-exercise)						
Stage	Minute	Speed (mph)	Grade (%)	HR (bpm)	BP	RPE
Resting	0-3	-	-			
Warm-up	3-8	3.0	0			
1	8-10	3.0	0			
2	10-12	3.0	2			
3	12-14	3.0	4			
4	14-16	3.0	6			
5	16-18	3.0	8			
6	18-20	3.0	10			
7	20-22	3.0	12			
8	22-24	3.2	12			
9	24-26	3.4	12			
10	26-28	3.6	12			
Post-Exercise	1 min	Dependent upon participant	-			
	2 min		-			
	3 min		-			
	4 min		-			
	5 min		-			

Table 3: Modified Balke Treadmill Test Protocol Sheet

APPENDIX B: ANCOVA REGRESSION ANALYSES

Table 4: Per-Protocol, ANCOVA Regression Analyses Assessing Effect of Exercise Training Type on Maternal Glucose Tolerance (Least Square Means)

	β	**SE**	**95% CI**	**p- value**
OGTT Serum Glucose (mg/dL)				
Exercise Type				
AT (n= 40)	-1.1	6.6	(-14.2, 11.9)	0.9
RT (n= 20)	1.3	7.9	(-14.3, 16.9)	0.9
CT (n=26)	-0.5	7.4	(-15.5, 14.2)	1.0
CON (n= 35) (referent)	-----	-----	-----	-----
Fitness Level				
Fit	10.7	6.4	(-2.0, 23.4)	0.09
Unfit (referent)	-----	-----	-----	-----
BMI	1.3	0.5	(0.3, 2.3)	0.01
Fasted maternal glucose in late pregnancy (mg/dL)				
Exercise Type				
AT (n=24)	-0.3	3.4	(-7.1, 6.4)	0.9
RT (n=20)	-3.3	3.5	(-10.2, 3.7)	0.4
CT (n=22)	-1.6	3.4	(-8.4, 5.1)	0.6
CON (n= 10) (referent)	----	----	----	----
Fitness Level				
Fit	-1.9	2.4	(-6.7, 2.9)	0.4
Unfit (referent)	-----	-----	-----	-----
BMI	0.4	0.2	(-0.1, 0.7)	0.1
Fasted Change in maternal glucose from mid-to-late pregnancy (mg/dL)				
AT (n=24)	-1.0	2.8	(-6.6, 4.6)	0.7
RT (n=20)	-6.3	4.1	(-14.4, 1.8)	0.1
CT (N=20)	-5.3	4.0	(-13.4, 2.7)	0.2
CON (n= 10) (referent)	-----	-----	-----	-----
Fitness Level				
Fit	-1.0	2.8	(-6.6, 4.6)	0.7
Unfit (referent)	-----	-----	-----	-----
BMI	-0.3	0.3	(-0.8, 0.2)	0.2

***Oral glucose tolerance tests were sampled from medical records. OGTT were performed between 25 and 27 weeks of gestation. Fasted maternal glucose in late pregnancy were measured at 36 weeks of gestation. Fasted change in maternal glucose from mid-to-late pregnancy measured the difference in between 36-week glucose measures and 16-week glucose measures. Fitness level was determined by relative VO_2 peak $mL.kg^{-1}.min$. Age was stratified in determining fit and unfit categories for participants VO_2.**
Groups represented: ≥ 80% exercise compliance

Table 5: ITT: ANCOVA Regression Analyses Assessing Effect of Exercise Training Type on Maternal Glucose Tolerance (Least Square Means)				
	β	**SE**	**95% CI**	**p- value**
OGTT Serum Glucose (mg/dL)				
Exercise Type				
AT (n= 64)	-2.1	5.3	(-12.6, 8.3)	0.7
RT (n= 25)	1.2	6.7	(-12.1, 14.4)	0.9
CT (n=33)	-1.9	6.2	(-14.3, 10.4)	0.8
CON (n= 45) (referent)	-----	-----	-----	-----
Fitness Level				
Fit	9.9	5.2	(-0.4, 20.2)	0.06
Unfit (referent)	-----	-----	-----	-----
BMI	0.9	0.4	(0.1, 1.9)	0.03
Fasted maternal glucose in late pregnancy (mg/dL)				
Exercise Type				
AT (n=31)	-2.2	2.7	(-7.7, 3.2)	0.4
RT (n=24)	-3.2	2.8	(-8.8, 2.5)	0.3
CT (n=23)	-2.6	2.9	(-8.1, 2.9)	0.4
CON (n= 16) (referent)	----	----	----	----
Fitness Level				
Fit	-0.8	2.1	(-5.0, 3.4)	0.7
Unfit (referent)	-----	-----	-----	-----
BMI	0.4	0.2	(0.03, 0.8)	.03
Fasted Change in maternal glucose from mid-to-late pregnancy (mg/dL)				
AT (n=31)	-3.4	3.2	(-9.7, 2.8)	0.3
RT (n=24)	-4.5	3.3	(-11.1, 2.1)	0.2
CT (N=21)	-5.5	3.3	(-12.1, 1.0)	0.1
CON (n= 16) (referent)	-----	-----	-----	-----
Fitness Level				
Fit	-0.5	2.5	(-5.4, 4.5)	0.9
Unfit (referent)	-----	-----	-----	-----
BMI	-0.2	0.2	(-0.7, 0.2)	0.3
***Oral glucose tolerance tests were sampled from medical records. OGTT were performed between 25 and 27 weeks of gestation. Fasted maternal glucose in late pregnancy were measured at 36 weeks of gestation. Fasted change in maternal glucose from mid-to-late pregnancy measured the difference in between 36-week glucose measures and 16-week glucose measures. Fitness level was determined by relative VO_2 peak $mL.kg^{-1}.min$. Age was stratified in determining fit and unfit categories for participants VO_2.**				

Table 6: Pairwise Composition Analyses Effect of Fitness Level on Maternal Glucose Tolerance (Least Square Means)				
	Mean	**Standard Error**	**95% Confidence Interval**	**p-value**
Clinical OGTT (mg/dL)				
Fit V Unfit	-10.1	5.1	(-20.2, -0.08)	0.04
Fasted maternal glucose in later pregnancy (mg/dL)				
Fit V Unfit	0.7	2.1	(-3.4, 4.8)	0.7
Fasted change in maternal glucose from mid-to-late pregnancy (mg/dL)				
Fit V Unfit	0.3	2.4	(-4.3, 5.0)	0.9