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Physical Activity During Pregnancy and Birth Outcomes in South Carolina 2009-2015

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PHYSICAL ACTIVITY DURING PREGNANCY AND BIRTH
OUTCOMES IN SOUTH CAROLINA 2009-2015

by

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DEDICATION

I dedicate this to the people who helped get me through graduate school, namely my parents, and the friends in my cohort, particularly Maggie and Christian. I would also like to dedicate this to my dog Gibb, who was very adamant throughout this process that his strict bedtime of 9:00pm was way more important than any work I needed to finish.

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I would like to acknowledge Dr. Liu for her experience and guidance throughout this lengthy and life-changing learning process, Dr. McLain not only for his participation in the thesis committee but for his intuitive approach to teaching biostatistics, and Dr. Boghossian for her expertise, commentary and keen attention to detail.

ABSTRACT

Physical activity is known to be beneficial to adults in general, including pregnant women, but the literature on physical activity and neonatal outcomes has been inconsistent. Few studies have differentiated between physical activity prior to pregnancy and during pregnancy to see whether the typical beneficial effect is not due to having a more active lifestyle in general.

The Pregnancy Risk Assessment Monitoring System (PRAMS) is a national cross-sectional surveillance system. Our data from SC PRAMS included 6391 respondents and was weighted to be representative of population of pregnant women that delivered in the state. We excluded births that were not singleton (n=624), births that were not viable (n=240), women with pre-existing diabetes (n=213) and women who had missing responses for our covariates(n=27), leaving a total sample of 5294 mother-neonate pairs. Database management and statistical analysis were carried out using SAS software version 9.4 (SAS Institute, Cary, NC). Our main analysis was carried out using logistic regression. All results were weighted to be representative of all live births from 2009-2015 in South Carolina and were considered significant at $p \leq 0.05$. We found that women who were previously inactive but became active during pregnancy had reduced odds of preterm birth (PTB) (aOR=0.54 (95% CI, 0.30-0.98)) compared with completely inactive women. We also found that women who did more exercise and for longer had lower odds of PTB. Conversely, we found women who had been active but stopped

activity had higher odds of PTB (aOR=1.5 (95% CI, 1.07-2.10)) and low birth weight (aOR=1.30 (95% CI, 1.03-1.62) than women who were inactive.

This analysis allowed a complex conceptualization of physical activity in a state representative population and demonstrated a dose response between PA and PTB but was subject to recall bias and did not have information on disability. In the future, prospective data collection should be used and exercise should be measured objectively.

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LIST OF ABBREVIATIONS

GA.....	Gestational Age
HBP.....	High Blood Pressure
LBW.....	Low Birth Weight
LGA.....	Large for Gestational Age
LTPA.....	Leisure-Time Physical Activity
METS.....	Metabolic Equivalent
PA.....	Physical Activity
PAI.....	Physical Activity Index
PTB.....	Preterm Birth
SGA.....	Small for Gestational Age

CHAPTER I

INTRODUCTION

1.1 BACKGROUND

While life expectancy has increased in the United States in the past century, an increase in the prevalence of chronic disease has hindered further gains in life expectancy¹⁻³. Lack of regular physical activity, a modifiable health risk factor, is a major cause of many common chronic diseases,¹⁻³ and has been estimated to contribute to 6% of the burden of coronary heart disease, 7% of type 2 diabetes, 10% of breast cancer, and 10% of colon cancer and to be associated with decreased life expectancy³. Conversely, physical activity has been associated with reduced risks for type 2 diabetes⁴, obesity⁵, depression⁶, anxiety⁶, and alzheimers⁷. People who are physically active also tend to be happier⁸, have better quality-adjusted life years⁹, and have better longevity and independence in old ages¹⁰.

While physical activity, as well as physical inactivity, is extensively covered in epidemiological literature, there's a great deal of variation as to how each are defined. Broadly speaking, physical activity can be defined as “any bodily movement produced by skeletal muscle that results in energy expenditure” (Caspersan, pg. 127)¹¹. Every single person performs some degree of physical activity though the amount each person does, varies based on the capability to do so and lifestyle preferences¹¹. Simple systems of categorization of physical activity include occupational physical activity, leisure time

physical activity, and activity during sleep, though this is not a large contributor to energy expenditure¹¹.

Exercise is a subset of physical activity “that is planned, structured, repetitive and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective” (Caspersan, pg. 128)¹¹. Generally, exercise is partaken during leisure time through sports, aerobic fitness, jogging, weight training, as well as many other activities, however certain occupational and household activities could also be considered exercise as long as they do not minimize work and are intended for this purpose¹¹. Because every person partakes in some forms of physical activity, and not all physical activity is of equal benefit, trying to define quantitatively what constitutes a “physically active” person is complex.

The *2008 Physical Activity Guidelines for Americans* were created by the US Department of Health and Human Services (DHHS) and define physical activity using two domains, aerobic and muscle strengthening exercises¹². The threshold for being a physically active adult that is set by these guidelines entails 150 minutes or more of moderate-intensity aerobic activity, or 75 minutes of more of vigorous-intensity aerobic activity per week, as this threshold is associated with substantial health benefit for cardiovascular disease and coronary heart disease¹². This is the same threshold recommended by the World Health Organization internationally¹³. The US guidelines also recommend that adults undergo muscle-strengthening exercises of moderate to high-level intensity at least twice a week¹².

For aerobic activity, these guidelines do not exclusively refer to physical activity during leisure time and may apply to occupational and household work of moderate or

vigorous intensity¹²⁻¹³. A study using the Behavioral Risk Factor Surveillance Survey System (BRFSS) data, found that within the aerobic standards of the guideline, 51.6% of adults engaged in 150 minutes of moderate aerobic physical activity, or 75 minutes of vigorous aerobic activity per week¹⁴. While physical activity, for conditions such as cardiovascular disease, has a clear dose response; increased duration of moderate and vigorous intensity aerobic exercise consistently results in decreased risk, this association is not consistent for all health outcomes^{12,13} and there may be health benefits for some outcomes below this threshold¹². Accordingly, not every study on the benefits of physical activity uses these guidelines to define someone as active, so what constitutes someone considered sufficiently physically active in research can vary. The aforementioned BRFSS study, while identifying that 51.6% of Americans were active by aerobic standards, found that only 20.6% of Americans met both aerobic recommendations and strength training recommendations¹⁴.

1.2 PHYSICAL ACTIVITY DURING PREGNANCY

Observational research on moderate to high intensity physical activity among pregnant women during pregnancy, since the early 1990s, has generally found neutral or beneficial health effects¹⁵. The American College of Obstetricians and Gynecologists (ACOG) currently recommends that most pregnant women with no pre-existing conditions adhere to the aerobic portion of the *2008 Physical Activity Guidelines for Americans* put forth by the DHHS, with the exception of certain forms of physical exercise such as contact sports, hot yoga and skydiving.¹⁶

Despite these recommendations, physical inactivity and inadequate physical activity is a problem among pregnant women. A 2004 BRFSS study found that 15.8%

(95% CI, 13.2-18.5) of pregnant women had “sufficient exercise” in 2000, defined at the time by 30 minutes of moderate leisure time physical activity 5 times a week, or 60 minutes of vigorous leisure time physical activity, compared with 26.1% (95% CI, 25.4-26.8) of non-pregnant women¹⁷. More recent physical activity recommendations differ slightly from the standard used at the time; the ACOG only started recommending moderate intensity exercises for at least 30 minutes a day, most(n=5) days of the week during pregnancy in 2002, which was later reduced in 2015 to from 20-30 minutes a day most days of the week.¹⁵

While there have not been more recent BRFSS studies examining the prevalence of physical activity in pregnant women using either the 2002 or 2015 ACOG guidelines, a recent 2016 NHANES study examined the difference in prevalence resulting from changing definitions¹⁸. Using 2007-2014 NHANES data, researchers found that, using the 2002 ACOG guidelines, 12.7% (95% CI, 6.9-22.2) of pregnant women had at least 150 minutes of exercise a week and exercised most days of the week, and that using the 2015 ACOG guidelines, 13.1% (95% CI, 8.7-19.8) had at least 100 minutes of exercise a week and exercised most days of the week.¹⁸ While the decreased ACOG threshold did not seem to substantially impact the prevalence of pregnant women meeting physical activity recommendations, when researchers changed the wording of the definition to include women who attained the physical activity threshold but did not exercise most days of the week, they found that 23.4% (95% CI, 14.9-34.9) of pregnant women had attained at least 150 minutes of leisure time physical activity a week¹⁸. In any case, pregnant women in the US appear to be less physically active than the US population as a whole. A physically active woman receives direct health benefits of physical activity,

mainly reduced comorbidities¹⁹⁻²², but a physically active pregnant woman also has reduced risk of pregnancy-related complications such as gestational diabetes²³. Poor maternal health²⁴ and maternal comorbidities²⁵ can impact the health outcomes of a newborn, so a physically active pregnant woman may see improved infant health outcomes due to the tendency for physical activity to improve overall health^{1,3} and reduce the risk of these comorbidities^{1,3}. While leisure-time physical activity (LTPA) is generally agreed to be beneficial to the general population¹², and most forms of LTPA are considered safe for pregnant women¹⁶, the literature is inconsistent as to whether the benefits of perinatal LTPA extend to infant health outcomes.

CHAPTER II

LITERATURE REVIEW

2.1 MATERNAL PHYSICAL ACTIVITY AND PRETERM BIRTH

Preterm birth, or preterm delivery, is commonly defined by a birth delivered prior to 37 weeks of gestational age, though it may also be subcategorized as moderate preterm (32-36 weeks), very preterm (28-32 weeks), and extreme preterm (<28 weeks)²⁶. This can be further described as spontaneous, where labor occurred or was indicated to have occurred due to medical indications such as partial premature rupture of the membranes, pregnancy-induced hypertension where labor was induced or caesarian section was used or both²⁷. Preterm birth is a condition that is associated with higher infant mortality with increasing prematurity^{28,29}. It also has been associated with several conditions in later life including increased risk for diabetes³⁰, attention deficit hyperactivity disorder (ADHD)³¹, cerebral palsy³², intellectual disability³³ and higher risk of disability^{32,33}. Examining the factors associated with preterm births may lead to better interventions and better recommendations to reduce the incidence of these health issues.

For our literature review about the association between physical activity during pregnancy and preterm birth, we reviewed all studies (n=27) used in Kahn's 2016 paper, "*Maternal Leisure-time Physical Activity and Risk of Preterm Birth: A Systematic Review*

of the Literature”³⁴. We restricted our analysis studies published in the last 10 years (2008-2018), 17 of which met this criteria³⁵⁻⁵¹. Five of these were randomized control trials³⁵⁻³⁹ and the remaining twelve were observational studies⁴⁰⁻⁵¹. Considering that we will use observational data for this thesis, the literature review is primarily focused on observational studies but the results of the randomized controlled trials will be discussed in brevity in the discussion.

These studies varied greatly in sample size, definitions of physical activity, and thoroughness of the study in assessing physical activity during pregnancy. We grouped these by study design type and then compared exposure and outcome definitions and findings and then compared them.

COHORT STUDIES

The cohort studies assessed included Hegaard (2008), Juhl (2008), Jukic (2012), Owe (2012), Tinloy (2014), and Currie (2014). Hegaard, Juhl and Owe found significant protective effects. These were large cohort studies, with the smallest (Hegaard) including 5739 participants⁴⁰ and the largest (Juhl) including 87232 participants⁴¹. Owe simply looked at the frequency of physical activity on, or prior, to certain weeks of pregnancy. Owe found that leisure time exercise, prior to 17 weeks of pregnancy, was associated with lower odds of having preterm deliveries (PTD), with an adjusted OR (aOR) of 0.89 (95% CI, 0.8-0.98) for exercise 1-2 times a week and with an aOR of 0.84 (95% CI, 0.75-0.93) for exercise 3-5 times a week compared with women who didn't exercise⁴³. This association was slightly stronger in those exercising prior to 30 weeks, with an aOR of 0.81 (95% CI, 0.73-0.89) at exercise 1-2 times per week, and an aOR of 0.76(95% CI, 0.68-0.86) at 3-5 times per week⁴³. Juhl compared hours of LTPA a week with no LTPA,

finding a hazard ratio (HR) of 0.82 ((95% CI, 0.76-0.88) for women that reported any LTPA compared with women who reported no LTPA, a HR of 0.8 (95% CI, 0.72-0.87) for women who reported between zero and one hours of LTPA a week compared with women who reported no LTPA, and a HR of 0.81 (95% CI 0.72-0.92) for women who reported between one and two hours of LTPA per week compared with women who did no LTPA⁴¹. Hegaard examined several thresholds of physical activity; ≥ 3 hours of light LTPA, ≥ 3 hours of moderate to heavy LTPA, as well as types of physical activity⁴⁰. Hegaard found that women involved with more than one type of sport had an aOR of 0.09 (0.01-0.66), and women who reported moderate to heavy LTPA, had an aOR 0.34(95% CI 0.14-0.85) compared with women not involved in sports or LTPA respectively⁴⁰.

Among the cohorts that did not find a significant difference, Tinloy set the minimum threshold for physical activity at 60 minutes a week, and only assessed late preterm birth (34 -<37 weeks gestation)⁴⁵; Jukic compared hard or very hard LPTA with women who did not have hard or very hard LTPA, using the Borg perceived exertion scale⁴²; Currie used a Kaiser Physical Activity Survey that aggregated multiple forms of physical activity, including LTPA, occupational physical activity and household activity⁴⁴.

CASE CONTROL STUDIES

Case control studies assessing physical activity and preterm birth have had mixed but generally favorable results⁴⁶⁻⁴⁸. We assessed three case control studies, Nelson (2009), Takito (2010), Guendelman (2013). These studies were of a similar size with the smallest being from Takito at 819 participants⁴⁷ and the largest being Guendelman⁴⁹

at 1042 participants. Nelson (2009) examined previously pregnant women in Thailand and did separate analysis for different types of physical activity and the period in which they were performed in⁴⁶. This included assessing women who were involved in exercise before, but not during pregnancy, before and during pregnancy, and during pregnancy, but not before pregnancy and compared these with women who participated in no exercise before or during pregnancy⁴⁶.

Nelson found that women who only exercised in leisure time prior to pregnancy, but not during pregnancy, had an aOR of 0.69 (95% CI 0.48-0.89) for preterm birth⁴⁶. Nelson also observed a non-significant reduction in point estimates for preterm birth risk for women who exercised before and during physical activity, at an aOR of 0.85 (95% CI, 0.59-1.24) compared with women who performed no exercise before or during pregnancy⁴⁶. Other forms of LTPA were also associated with reduced point estimates, but not significantly⁴⁶. Conversely, the study found found substantial and significant increases in the odds of preterm delivery for women who reported that their job during pregnancy involved heavy exertion “such as physically stressful work including lifting or carrying objects or loads >25kg as in construction work”⁴⁶. These women had an overall aOR of 2.42 (95% CI, 1.15, 5.09) of preterm birth compared with women who did not, and also had higher odds of very preterm delivery (<32 weeks) at an aOR of 4.57 (95% CI 1.65, 12.64), as well as medically indicated preterm delivery at an OR of 3.79 (95% CI, 1.54, 9.32)⁴⁶. All adjusted analysis by Nelson controlled for maternal age, pre-pregnancy BMI, and parity, and where occupational physical activity was examined, the analysis was restricted only to women who were employed during pregnancy⁴⁶.

Takito (2010) found that, in the unadjusted model, light leisure physical activity was beneficial, but after adjustment for maternal education, marriage status, age, paid work, high blood pressure, early rupture of membranes, hospitalization, bleeding and antenatal consultation the association disappeared⁴⁷. The study did find, in the adjusted analysis, that leisure walking under 20 minutes a day was associated with an aOR of 0.44 (95% CI, 0.21-0.90) and over 20 minutes a day was associated with an aOR of 0.36 (95% CI, 0.17-0.89) for preterm birth compared with women who did not have any leisure walking⁴⁷. They also found that domestic activities, essentially housework, at over 6 hours a day, was associated with an aOR of 0.38 (95% CI, 0.17-0.89) for preterm birth, compared with women that performed under two hours of domestic activities a day⁴⁷.

Gruendelman (2013) found that women who reported having engaged in hours of moderate physical activity, and vigorous activity, modeled continuously, had reduced odds of preterm birth in the crude model⁴⁸. After adjustment the only association that remained was for moderate activity at an aOR of 0.91 (95% CI 0.81-0.98)⁴⁸. This study is notable as it found effect modification by BMI in pregnant women⁴⁸. Each one unit increase in pre-pregnancy BMI was associated with an OR of 0.87(95% CI 0.80-0.94) for preterm birth up to a BMI of 24, and an OR of 1.07 (95% CI, 1.03-1.12) for preterm birth per one unit increase in BMI for women at 24 BMI or greater⁴⁸.

CROSS-SECTIONAL STUDIES

Cross-sectional studies, assessing whether physical activity had a protective effect on preterm birth, also had inconsistent results⁴⁹⁻⁵¹. We reviewed three studies, Domingues (2008), Dumith (2012), and White (2014), which ranged from 284 participants (White), to 4147 participants (Domingues). Domingues sampled from a birth cohort and was the

only one of these studies to find that physical activity lead to a significant reduction of odds of preterm birth. It was also the most thorough of the three, assessing physical activity by duration and trimester, but did not distinguish between type of physical activity and intensity. Domingues (2008) found significant adjusted prevalence ratios (aPR) for women who underwent LTPA in all three trimesters (aPR: 0.55, 95% CI 0.32-0.96), for women who that participated in LTPA in their third trimester (aPR: 0.50, 95% CI 0.31-0.80) and for women that participated in more than 90 minutes of LTPA a week in their third trimester (aPR: 0.58, 95% CI 0.34-0.98) compared with women who did not partake in LTPA.

Dumith (2012) used a hospital-based, cross sectional study, which utilized an adjusted analysis, controlling for schooling, marital status, maternal age, income, parity, prenatal consultation and twins, however the extent of the exposure ascertainment was assessed entirely by the question “Did you practice physical exercises during this pregnancy?”⁴⁹. The findings suggested no association with preterm birth at an aOR of 0.98 (95% CI, 0.79-1.22) for preterm birth⁴⁹.

White (2014) recruited from surveys given to Anytime Fitness members and defined physical activity by separate groups that performed (5 minutes/day a week) of resistance exercise and aerobics (10 minutes/ day a week), aerobics but no resistance exercise, and those with no exercise⁵¹. The main outcome of interest was gestational age at delivery which used a referent category of 37-40 weeks of age at delivery with a category combining preterm (≤ 36 weeks) and postterm (≥ 40 weeks) delivery. The analysis was carried out through a contingency table and logistic regression. Two tables were used, one that examined all three categories of physical activity with type of

gestational delivery($p=0.85$), and one that compared resistance training/aerobic training with a combination of aerobic training and no exercise($p=0.66$). The logistic regression included all three PA exposure levels, and while there was a point estimate suggesting a protective effect for resistance training/aerobics on preterm labor (aOR 0.59, 95% CI, 0.27-2.29) compared with no exercise. The study did not present findings on physical activity and preterm birth using logistic regression as the outcome “showed poor fit to the data”⁵¹.

SUMMARY

Randomized control trials that set women to exercise routines did not find significant differences in preterm birth³⁵⁻³⁹. Of the twelve observational studies detailed⁴⁰⁻⁵¹, five found no differences between physical activity, either before or during pregnancy^{42,44,45,50,51}, and seven found some significant protective effects for some level or type of physical activity^{40,41,43,46-49}.

Generally speaking the cohorts that did not find an association were smaller^{42,44,45}. The largest cohort that found no difference was “*Exercise during pregnancy and risk of late preterm birth, cesarean delivery, and hospitalizations*” by Tinloy (2014)⁴⁵, and had 3006 participants whereas smallest cohort study that found a difference was “*Leisure time physical activity is associated with a reduced risk of preterm delivery*” by Hegaard (2008) and had 5749 participants⁴⁰. Two^{41,43} of the three cohorts^{40,41,43} that found associations between physical activity and reduced preterm birth assessed frequency of physical activity, or length of physical activity, compared with no physical activity, rather than relying on a predetermined threshold^{45,47}. The exception was Hegaard which assessed women to be physically active at three hours, or over, of light, or moderate to

heavy physical activity⁴⁰. In Hegaard, while women who engaged in light LTPA(>3h/w) had point estimates indicative of a protective effect on preterm birth, at an aOR of 0.76 (0.60-1.02) compared with women who were not physically active, only women engaging in moderate to heavy LTPA(>3h/w) had significantly reduced odds of preterm birth, aOR of 0.34 (0.14-0.85) compared with women who were not physically active⁴⁰.

The definition of the outcome, preterm birth, was defined as <37 weeks in nearly all observational studies, with two exceptions^{45,51}. Tinloy examined only late preterm birth (34-<37 weeks)⁴⁵, and White aggregated preterm (≤ 36 weeks) and postterm (≥ 41 weeks) into one outcome⁵¹.

Among case control and cross-sectional studies, four⁴⁶⁻⁴⁹ out of the six⁴⁶⁻⁵¹ found that some form of perinatal physical activity, was associated with reduced odds of preterm birth. However, Nelson only found significance with exercise *prior* to pregnancy after adjustment⁴⁶, and Takito only found walking (not LTPA in general) and domestic physical activity (over 6 hours/day) during pregnancy to be protective against preterm births in the adjusted model⁴⁷. Gruendelman, like the cohort by Hegaard⁴⁰, only found *moderate* physical activity to be significantly associated with reduced preterm birth after adjustment⁴⁸.

DISCUSSION

One might expect that the lack of significant findings from randomized control trials to be definitive evidence against the efficacy of preterm birth, but as Kahn suggested, there's an issue of a "healthy mother effect" where participants in a voluntary clinical trial may have better socioeconomic status, be excluded for certain health conditions, and may be healthier participants than in the general population³⁴. This would

attenuate the differences between the groups, and randomization of cases and controls would not be able to fully address this issue, which limits generalizability to the population as a whole³⁴. Compared with cohort studies, a randomized control trial is also likely to have a substantially smaller sample size due to higher costs and logistic feasibility, and in comparison, less statistical power to detect differences.

The majority of these observational studies used self-reported data but conceptualized physical activity differently, which may explain some of the inconsistent findings. There might be some physical activities that show clear benefits at a low threshold compared with others. Takito for example, found leisure walking to be associated with lower odds of preterm birth at even less than 20 minutes a day (aOR 0.44 (95% CI 0.21-0.91)), compared with women who did none, which had a similar protective effect to women engaging 6 hours of domestic physical activity a day (aOR 0.53 (95% CI, 0.31, 0.89)), compared with women who did 2.5 hours or less⁴⁷.

Currie's methodology assumes all exertion in all domains of physical activity, including leisure time exercise, occupational activity and active living are equally beneficial in preventing preterm births, as they are equally weighted and aggregated in terms of MET⁴⁴. Part of the findings in Nelson indicate that the methodology used in Currie may not be justifiable. If the general assumption is that moderate to heavy LTPA is associated with reduced risk of preterm birth, such as in Hegaard, (aOR = 0.34 (95% CI, 0.14-0.85))⁴⁰, and high physical occupational exertion such as in Nelson is associated increased preterm birth (aOR 2.42 (95% CI 1.15-5.09))⁴⁶, in an aggregated model this would average out towards the null even if there were clear associations when examined separately.

All studies except White (2014) and Tinloy(2014), defined the outcome of preterm birth/delivery as a birth estimated at <37 weeks of gestational age, suggesting that differential outcome classification was not a concern for the most part. The issue with White's method of aggregating pre-term and post-term births is simple, at least conceptually, as it's only defensible assuming a bidirectional effect towards, or away from, the reference group. A protective effect on pre-term birth, but not post-term birth, or vice versa, would attenuate the strength of the association. A consistent one direction effect on gestational age might also, for example, reduce the risk of preterm birth, but simultaneously increase risk of post-term birth with no net change in odds.

Tinloy, meanwhile, examined late preterm birth (34-<37 weeks of gestational age) exclusively, as the study inclusion criteria excluded pregnant women under 34 weeks of gestational age. This resulted in non-significantly elevated point estimates at 60-149 minutes of PA a week for late preterm birth (aOR 1.14 (95% CI, 0.71-1.84)) compared with women who did under 60 minutes of PA⁴⁵. There are several plausible reasons for this. The simplest is that physical activity during this period of pregnancy does not confer a reduced risk of late preterm birth, as the definition used by Tinloy to determine PA asks about *current* weekly physical activity⁴⁵. If a clear beneficial effect on preterm birth occurs from LTPA before pregnancy, or early in the pregnancy, but not late in the pregnancy, this could potentially bias results. At recruitment at 34 months of the pregnancy, the progression of infant development may make LTPA uncomfortable, resulting in women to cease to be considered physically active. They may have already benefited from pre-pregnancy activity, causing the reference group to be at similar health as women who are active at the inclusion into the study. However, when Gruendelman

conducted an analysis separately using late preterm birth (35-36 weeks of gestation) and early preterm birth (<35 weeks of gestation) compared with term births, the association remained similar, both separately and jointly⁴⁸.

The method of adjustment may play a role in the differences in findings as well. Tinloy⁴⁵, for example, was the only observational study that adjusted for a history of hypertension, but as Domingues pointed out, high blood pressure is a physiological cause of preterm birth and is reduced by physical activity⁴⁹ and is therefore an intermediate variable in the association and may not be appropriate to control for. Guendelman also revealed a potential concern with how pre-pregnancy BMI is conceptualized by finding effect modification by BMI category⁴⁸, which was based upon previous research the author performed⁵². Both studies found that the risk of preterm birth increases from 24 BMI^{48,52}.

Another gap in this literature was brought up by Kahn, as well as Guendelman; the benefits of LTPA during pregnancy may be due to long term benefits of LTPA, such as LTPA before pregnancy, rather than necessarily LTPA performed in any period of pregnancy^{34,48}. Of all of the observational studies reviewed on PTD, only Nelson and Currie⁴⁴ examined PA before and during pregnancy, and only Nelson examined LTPA⁴⁶. The findings by Nelson were supportive of this hypothesis, as the protective effect of LTPA on moderate preterm birth was only observed in women who exercised before pregnancy (aOR 0.70 (95% CI, 0.52-0.94)), and women who were only physically active before, but not during pregnancy (aOR 0.67 (95% CI 0.46-0.97)), though point estimates indicative of a protective effect (aOR < 1.0) were generally observed in women who engaged in LTPA both during and before pregnancy⁴⁶. Women who were active only

during pregnancy had a slightly elevated risk of preterm birth, (aOR 1.29 (95% CI, 0.40, 4.13), but this group consisted of a very small number of women (n=14) and should be interpreted with caution⁴⁶.

2.2 MATERNAL PHYSICAL ACTIVITY AND BIRTHWEIGHT

When it comes to health outcomes and birth weight, we are primarily concerned with measurements that deviate substantially from the mean birth weight, in either direction, such infants born too small or too large. The diagnostic definition in the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) for low birth weight is a birth weight below 2500 grams⁵³, but there are also subcategories of low birth-weight, such as very low birth weight at less than 1500 grams⁵³, and extremely low birth weight at 999 grams or less⁵³. The “opposite” problem is fetal macrosomia, which is typically defined by a birth weight at or above 4000 grams⁵⁴. Both conditions have been shown, in previous literature, to be associated with adverse health outcomes; low birth weight has been associated with higher infant mortality⁵⁵ and lower academic performance later in life⁵⁶, whereas macrosomia has been associated with obesity⁵⁷⁻⁵⁸, cardiovascular issues⁵⁸ and insulin resistance⁵⁷.

When only assessing low birth weight in live births, it may be due to a variety of exposures, but also may be due to prematurity, where the newborn was simply born earlier in development than other infants. Accordingly, many birth weight outcomes are assessed in terms of weight adjusted for gestational age.

Classification of weight for gestational age, like birthweight is bimodal, with newborns being classified as either small for gestational age (SGA), average for gestational age (AGA), or large for gestational age (LGA). SGA has been traditionally

defined as a birthweight in the lowest 10th percentile for the newborn's gestational age while LGA is classified as the top 90th percentile for gestational age using a particular reference population^{59,60}. However, this system of classification has been criticized as arbitrary and more useful for clinical classification than for research, as certain health effects may become evident above or below the 10th and 90th percentile thresholds⁶⁰, so studies may define SGA and LGA by different percentiles. It should be taken into consideration that the specific distribution of the reference population may also vary by biological sex, parity, or race, so what constitutes a low birthweight girl may be different from what constitutes a low birthweight boy⁶⁰.

For our literature review about the association between physical activity before or during pregnancy and birth weight outcomes, we reviewed all articles (n=54) from Bisson's 2016 systematic literature review, "*Physical Activity Volumes during Pregnancy: A Systematic Review and Meta-Analysis of Observational Studies Assessing the Association with Infant's Birth Weight.*" We restricted our analysis to articles (n=24)^{42,44,47,50,62-82} published in the past 10 years (<2008) to reduce the work scope.

We additionally excluded four studies (Morgan (2014), Mäkelä (2013), Reid (2014) and Mparmpakas (2013)) because they did not directly conduct an analysis of the association between physical activity before or during pregnancy and birth weight outcomes.⁶²⁻⁶⁵ While Mahmoodi (2013) used a direct comparison between LTPA measures and low birth weight, the point estimate of the odds ratio was outside of the bounds of the confidence interval, leading us to exclude it as well⁶⁶. In total we analyzed nineteen studies^{42,44,47,50,66-82}. As we had a number of different types of outcomes relevant to birth weight, we categorized these by outcome for the sake of simplicity.

CONTINUOUS BIRTH WEIGHT

Eight studies assessed continuous birth weight in grams either, using bivariate analysis between groups, or through a regression model^{42,67-74}. Five^{42,67,68,70,73} out of the eight found an association between a form of physical activity and a continuous birth weight, three did not^{71,72,74}. Among the five studies that found a significant association between physical exercise and birth weight in grams, four found that exercise status was associated with reductions in birth weight^{42,68,70,73} and one found increased birth weight⁶⁷. All of these studies used a cohort study design.^{42,67-74}

As previously discussed, it's important to look at the context of the study, as the infants gestational age can play a role in its birth weight. These studies generally addressed confounding from gestational age in some way, with the exception of Jukic⁴² but the method and extent varied. Many utilized some exclusion criteria that would prevent or mitigate the skew of preterm births on the analysis. Hegaard, and Fleten excluded preterm births (<37 weeks)^{69,73}. Melzer included only women above 35 weeks of pregnancy⁷². Jahromi only included women above 33 weeks of pregnancy⁶⁷. Some of the exclusion criteria did not exclude preterm births; Monpetit only included women at or above 18 weeks of gestational age⁷⁰ and Both excluded the only women (n=1) delivering prior to 16 weeks. Finally, Harrod did not exclude women but adjusted birthweight for gestational age⁶⁸.

Monpetit(2012) and Melzner(2014) were the only two studies included in the literature review that measured physical activity objectively^{70,72}. Both of these were small studies Melzner (n=44) and Monpetit (n=59) that measured and defined physical activity differently and had different results. Monpetit measured physical activity with a

pedometer, defining it in terms of steps, finding that, per 1000 steps per day, birth weight dropped by 0.78g (p=0.044). This association lost significance after adjusting for pre-pregnancy BMI⁷⁰. Melzner measured physical activity with a heart rate and motion sensor, considering women physically active at 30 minutes of exercise at 3.0-6.0 METS per day, and inactive under this threshold, and found no association⁷².

Fleten defined exercise exposure by frequency per week and found that the strength of the association between exercise and birth-weight reduction varies by the gestational week that the woman was physically active. The national birth cohort that Fleten used sent out questionnaires at 17 and 30 weeks to examine a woman's exercise habits before 17 weeks and between week 17 and 30⁷³. The strength of the association was stronger for exercise between weeks 17-30 of gestation where birth weight was reduced -1.4g (-2.01 to -0.78) per exercise in the adjusted model, but a significant association was also seen prior to week 17, with birth weight reductions of -0.72g (-1.33 to -0.10) per exercise in the adjusted model⁷³. Fleten and Monpetit were the only studies that assessed the relationship between PA and BW using regression models^{70,73}

Harrod (2014), Jahromi(2011), and Jukic (2012) assessed differences in mean birth weight between groups of women who were physically active and not physically active. Harrod assessed METs by quartiles and found that the top 25th percentile of physical exercise had significantly (p=0.04) lower mean birth weight (3,142.9g) than the bottom quartile (3,239.9g)⁶⁸. Jukic found women engaging in non-vigorous leisure time physical activity had an average birth weight reduction of -60g (-117 to -1) and that women who had between 1 and 75 minutes of vigorous leisure time activity had an

average birth weight reduction of -96g (-192 to -0.2) compared with women who engaged in no leisure time physical activity during pregnancy⁴².

Jahromi, unlike the majority of papers examining this topic, found that women had higher mean birth weights if they exercised before (3210g vs. 2880g) and during pregnancy (3230g vs. 2910g) than women who did not⁶⁷. Both (2010), Hegaard (2010), and Melzer (2010) meanwhile found no association between birth weight in grams and exercise status^{69,71,72}.

LOW BIRTH WEIGHT AND MACROSOMIA

Seven studies examined macrosomia or LBW as an outcome^{44,47,50,69,71,76,82}. Of these, three assess both macrosomia and LBW^{44,69,76}, two assess only macrosomia^{75,82}, and two assess only LBW^{47,50}. Of these seven studies, four were prospective cohorts^{44,69,75,82}, two were cross sectional^{50,76}, and one was a case control study⁴⁷. Two of the four cohort studies^{75,82} and the case control study⁴⁷ found physical activity to have a significant protective effect of PA on LBW or macrosomia, however no cross sectional study found significant differences^{50,76}.

The studies that examined role of physical activity in both macrosomia and LBW were Hegaard(2010), Wojtyla(2012), and Currie (2014) the first two of which found no significant association^{44,69,76}. Using the Kaiser Physical Activity Survey(KPSA), Currie found that the top tertile of physical activity had an adjusted OR of 0.61 (95% CI, 0.43-0.85) for macrosomia compared with the lower tertile, but no other significant differences⁴⁴. This analysis did not exclude births <37 weeks of estimated gestational age, but the authors conducted a sub-analysis and claimed that excluding these births did not change the results⁴⁴.

The studies that only examined macrosomia, Voldner (2008), and Owe (2009) both found a significant protective effect of exercise on odds of macrosomia^{75,82}. Voldner found, using a prospective cohort, that women who exercised up to or less than an hour per week had an increased risk of macrosomia (aOR of 2.9 (95% CI, 1.2-7.3)) compared with women who exercised more than an hour a week. However, this effect was significant only prior to pregnancy, not during pregnancy⁸². Owe assessed physical activity in terms of “active transport” such as walking, jogging and biking, and frequency of this activity, and determined that women who exercise prior to 17 weeks of pregnancy 3 times a week had an aOR of 0.72 (0.56-0.93) of macrosomia (defined as >4170g in nulliparous women, and >4362g in multiparous women) compared with women who did not⁷⁷. This association slightly attenuated women exercising prior to 30 weeks of pregnancy, three times a week, with an aOR of 0.77 (95% CI, 0.61-0.96)⁷⁵.

Takito (2010) and Dumith (2012) examined low birth weight, but not macrosomia^{47,50}. Dumith assessed any leisure time physical activity during pregnancy and LBW and found no association⁵⁰. Takito used a survey that differentiated between subdomains of physical activity, while there was no association between LTPA and LBW, he found that women who reported over 7 hours of light physical activity had an aOR 0.61(95% CI, 0.39-0.94) of LBW compared with women who did under 3.5 hours⁴⁷. It was also found that women who reported 4-5.9 hours of domestic physical activity had an aOR of 0.6(95% CI,0.36-0.98) of LBW compared with women who did under 2 hours⁴⁷.

SIZE FOR GESTATIONAL AGE

Six studies examined the outcome of size for gestational age^{68,74,77,79-81}, of these, half assessed both SGA and LGA^{74,77,79}, two assessed only SGA^{68,80}, and one assessed only LGA⁸¹. Five of the six found an association with the exception of Portela (2014) which, as it was a cohort study with 56 people, had zero cell count for these outcomes and was unable to draw a conclusion⁸². The remaining five studies consisted of four cohort studies^{68,74,77,80} and a cross sectional study⁸¹. The findings of the studies, that were able to draw conclusions, were mixed, with three studies showing a significant protective effect for physical activity on SGA or LGA^{74,77,81}, one showing both significant protective and deleterious effects for SGA depending on type of PA⁸⁰, and one showing only deleterious effects for SGA⁶⁸.

Juhl(2010), assessed the frequency and duration of physical activity, compared with none, and found increased LTPA to have a slight protective effect for both SGA and LGA. While the greatest protective effect was found for both LGA (HR 0.72, 0.57-0.91) and SGA (HR 0.83, 0.72-0.95) at 3-5 hours a week, a smaller but significant effect on both LGA (HR= 0.93, 0.88-0.98) and SGA (HR= 0.88, 0.83-0.93) was observed at less than one hour of exercise a week⁷⁴.

Mudd used a pre-existing cohort study called the POUCH Cohort which sampled from the general population but over-sampled women with high maternal serum alpha-fetoprotein (MSAFP) levels, among other things, as a sub-cohort⁷⁷. He then mailed out questionnaires about frequency and duration of physical activity and found that women in the “non-sub-cohort” who reported that they received over 150 minutes of exercise a week had significantly reduced odds (aOR=0.30 (95% CI, 0.14-0.64)) for LGA compared

with women who did not⁷⁷. Snapp (2008), performed an unadjusted analysis on national survey data, classifying women as physically active if they partook in leisure time physical activity for at least 30 minutes, three times per week or more, for six or more months of the pregnancy. Snapp found that women who were not physically active had an OR of 12.9 (95% CI 10.9–15.2) for LGA compared with women that were⁸¹. It should be noted that LGA was defined at 95th percentile of weight, and that women delivering before 37 weeks were not included.⁸¹

Gollenburg (2011) used a Kaiser Physical Activity Survey (KPSA) and found that before pregnancy, women at 75th percentile and higher in total physical activity had reduced risk (RR= 0.42 (95% CI 0.21-0.82)) of SGA births compared with women at or under the 25th percentile. However, women at or over the 75th percentile for sports and exercise were at increased risk (RR=2.14 (95% CI, 1.04-4.39)) of SGA births compared with women at or under the 25th percentile⁸⁰. Harrod (2014) also used a survey that aggregated all types of physical activity, the Pregnancy Physical Activity Questionnaire, similarly arranged it into quartiles, but found that, in late pregnancy, compared with the referent <25th percentile MET group, the 25th-50th percentile MET group had increased odds of SGA birth (OR 2.2 (95% CI, 1.1-4.3)), and the 75th -100th percentile MET group also had increased odds of SGA birth (OR 3.0 (95% CI, 1.4-6.7)) when compared to the same reference group⁶⁸.

SUMMARY

All of the studies that we reviewed (n=19) on this PA and birth weight outcomes were prospective cohort studies, or based on prospective cohort studies⁷⁷, with the exception of Takito (2010) which was a case control study, Wojtyła (2012), Dumith

(2012) and Snapp (2008) which were cross sectional studies. Among studies that examined birth weight as a continuous variable or mean, the majority suggested that physical activity and LTPA were generally associated with lower birth weights, with one exception⁶⁷. Six studies examined physical activity and outcomes of macrosomia. Voldner(2008), Owe (2009), and Currie(2013) found that physical activity reduced odds of macrosomia, which is consistent with the reduction in birth weight in grams found in the literature examining that outcome.

Among the five studies that assessed low birth weight, only Takito (2010) found that physical activity was protective of LBW, and then only for domestic and light physical activity rather than LTPA. Finally, six studies^{68,74,77,79-81} assessed SGA and/or LGA. Juhl (2010) was the only study where LTPA reduced risk of both SGA and LGA with a protective linear effect on both SGA and LGA⁷⁴. Every study that examined and LGA, reported that physical activity decreased odds of LGA birth. The two studies that only examined outcomes of SGA, reported increased odds of SGA birth among women were physically active during mid/late pregnancy^{68,80} however one of these also reported decreased odds of SGA for women physically active before pregnancy⁸⁰.

DISCUSSION

While we did not review the majority of the literature provided in Bisson (n=54), as a whole, it was generally indicative that physical activity was protective against LGA and macrosomia in newborns, where it was not, physical activity was rarely found to be detrimental. In Bisson, the author indicates finding generally high heterogeneity among studies ($I^2 = 0.87$) and presented similar findings⁶¹. Nevertheless, there were a number of

methodological differences and limitations in a number of studies that may explain some of the inconsistencies in results.

Most of the studies we examined from Bisson⁶¹, similarly, to the meta-analysis by Kahn, used some form of self-reported physical activity data. The exceptions to this were Monpetit (2012), and Melzer (2010) which both used objective data collection^{70,72}. There were substantial differences among these studies in physical activity was collected and defined, but they generally were classified by daily or weekly duration of the PA, frequency of PA per week, the type of PA and its intensity.

It's not clear how the method of determining physical activity by use of MET (intensity by hour by week) or categorization by standards similar to ACOG (frequency/week by minutes/week) affect the outcome, as no study reviewed appeared to have compared these methods.

A minority of studies examined whether there were different outcomes from PA during different stages of pregnancy, and/or examining a woman's PA habits before pregnancy. Hegaard (2010), Gollenburg (2011) and Harrod (2014) were the only studies that examined physical activity in multiple stages of pregnancy to compare risk^{68,69,80}. The time frames these studies examined were fairly similar; Hegaard recorded PA before 16 weeks of gestation and before 30 weeks of gestation, Gollenburg recorded PA before recruitment (mean=15 wks), and on follow-up (mean=28 wks), and finally, Harrod recorded PA on early pregnancy (median=17 wks), late pregnancy (median=27 wks) and during hospitalization.

Gollenburg (2011) and Harrod (2014) were noteworthy as being the two studies that found significantly higher rates of SGA births with some form of physical activity^{68,80}.

Harrod aggregated MET/hours of total energy expenditure separately during early, mid pregnancy and late pregnancy whereas Gollenburg used a survey that examined different types of physical activity (occupational, sports, household) during early and middle pregnancy, but both studies assessed these scores by quartiles of scores^{68,80}.

While the point estimates on SGA birth in early pregnancy in both Harrod and Gollenburg were generally indicative of a protective effect, there was a significant increase in SGA birth in the latest period of pregnancy for both studies^{68,80}. Gollenburg found that women in the 2nd and 4th quartiles of sport and exercise during mid pregnancy had an increased relative risk for SGA birth at respectively 2.88 (95% CI, 1.41-5.9) and 2.14 (95% CI, 1.04-4.39) compared with the 1st quartile. Harrod found that women in the 2nd and 4th quartiles of total MET-hrs/week during late pregnancy had an increased odds of SGA birth at respectively 2.2(95% CI, 1.1, 4.3) and 3.0(95% CI, 1.4, 6.7) compared with the 1st quartile.

While Hegaard did not find an effect in the third trimester by hours of sport, there were elevated point estimates for different classifications of sports. Hegaard found that women who gave delivery to term babies (>37 weeks), and who were involved in one weight carrying activity (including aerobics, dancing, and running) in the third trimester had an aOR of 1.6 (95% CI, 0.5-5.6) for LBW birth compared with women who did no sport and women who were involved in other sports activities (karate, horse riding, yoga, rowing) had an aOR of 1.9 (95% CI, 0.7-5.1) compared with women who did no sport⁶⁹. The general implication from these two studies, is that during later periods of medium and high levels of sports and exercise may increase risk of SGA births. While the findings from Hegaard were insignificant they generally support this concept.

As previously discussed, Kahn and Guendelman noted that the benefits of LTPA during pregnancy may be due to long term benefits of LTPA, such as LTPA before pregnancy, rather than necessarily LTPA performed in any period of pregnancy^{34,48}. Four studies in this review examined pre-pregnancy physical activity. These were Gollenburg(2011), Koushkie(2014), Currie (2014) and Voldner(2008), who respectively examined the outcomes of only SGA, mean birth weight, LBW and macrosomia, and only macrosomia.

Gollenburg generally saw reduced point estimates for SGA in pre-pregnancy for all forms of physical activity, except household work, but the only significant reductions in SGA risk, for this category, were in third quartile of sports/exercise (RR= 0.56 (95% CI, 0.33-0.96)) and in the second quartile of total activity (RR= 0.57 (95% CI, 0.33-0.98)) compared with their respective first quartiles. Koushkie found no difference in mean birth weight but attributed this to the fact that 97% of women who were physically active were physically active during both periods of pregnancy⁶⁷.

Though none of the outcomes for pre-pregnancy PA were significant for Currie, the point estimates indicative of reduced risk of LBW and macrosomia were found with the second tertile of KPAS score compared with the first⁴⁴. Voldner found that women who exercised less than 1 hour per week had roughly 3 times (aOR 2.9 (95% CI, 1.2-7.3)) the odds of macrosomia as women who exercised more than 1 hour per week⁸², concurring with the trend.

The findings from Voldner, Gollenburg and Harrod suggest the perinatal period in which the woman is physically active may result in different odds of birth weight outcomes^{68,80,82}. This may explain a number of insignificant findings from papers in the

Bisson review, as there may be a benefit of physical activity on birth weight outcomes during pre-pregnancy and during early periods of pregnancy, but risk during later periods. Studies that do not attempt to differentiate between these may have end up with results biased towards the null.

As previously discussed in this paper, and indicated by the literature, different forms of physical activity may result in a different effect on birth outcomes. This may explain why Currie saw no effect of pre-pregnancy physical activity on birthweight outcomes while Gollenburg did, despite both studies using the same survey. Currie did not assess LPTA, and instead simply aggregated all subdomains of physical activity⁴⁴ while Gollenburg differentiated between subdomains including LTPA⁸⁰.

Out of the nineteen papers we reviewed, only Gollenburg and Voldner examined pre-pregnancy LTPA and only for, respectively, SGA and macrosomia^{80,82}. This suggests inadequate literature for effect of pre-pregnancy LTPA on SGA and macrosomia, and a gap in literature on the effect of pre-pregnancy LTPA on LGA and LBW.

The different definitions used for outcomes may have played a role in different results as well. Hegaard's insignificant findings between LTPA and macrosomia may be attributable to setting the definition of macrosomia as birth weight at or over 4500g, or 300g higher than Voldner's threshold and 330g higher than Owe's threshold, both of which did find a significant difference. Snapp's definition of LGA at the 95th percentile, as well as defining a woman as physically active at 30 minutes of exercise 3 times a week, for at least 6 months of pregnancy, may have also contributed to having a disproportionately high calculation of risk (OR=12.9 (95% CI 10.9–15.2)) for women who did not meet this threshold, particularly as it was unadjusted for BMI or any other

factor and excluded preterm deliveries⁸¹.

We saw similar gaps in the literature as we did in the section on preterm birth. Only two studies assessed specifically LTPA before pregnancy, which was indicated to be a concern in Kahn³⁴, but each used different methods of calculating LTPA and exercise, and, only one birth weight outcome was assessed in each study.

2.3 EFFECT MODIFICATION

Though race and BMI are commonly viewed as confounding factors in the association between physical activity and birth outcomes, only Guendelman examined pre-pregnancy BMI as an effect modifier in their main analysis⁴⁸. While normal range (18-24.9 BMI) BMI is generally considered the referent category for health risk, BMI has been previously found to have a V shaped distribution for risk of preterm birth with the lowest odds centered around 24 BMI⁵² increasing sharply to an OR of 4.31 (95% CI 1.94-9.54) by 17 BMI and increasing gradually to a similar OR at around 37 BMI⁵².

Additionally, no study reviewed in this paper conducted a sub-analysis on race specifically. This is pertinent because minority groups, and particularly African Americans get less leisure time physical activity than their white counterparts⁸³ and have worse birth-weight outcomes⁸⁴. In a population with a large ethnic minority, we may find that race modifies the effect between physical activity and birth outcomes. Only three studies contained large (>10%) non-white populations^{67,77,80}, but of these, only one of these were a minority group within the overall population where the study took place⁷⁷. None of these adequately addressed whether preterm birth or birth weight may vary by race.

2.4 GENERAL PROPOSAL

The Pregnancy Risk Assessment Monitoring System (PRAMS) is a national cross-sectional surveillance system carried out through a collaborative effort between the CDC and state health departments, on a yearly basis. The survey recruitment is based on, and therefore linked to, newborn's birth certificate data, which includes information on delivery and measurements of gestational age and infant weight. PRAMS also includes self-reported information on various topics such as access to prenatal care and health behaviors before and during pregnancy.

The SC PRAMs survey is unique nationally because only two other states collect information on physical activity during pregnancy (Colorado and North Carolina) and no other states use more questions than South Carolina on the topic of physical activity. These questions assess physical activity before, as well as during, pregnancy, provide information on the duration of the pregnancy that the woman was physically active, and allows respondents to specify the type of exercise they most frequently participated in, which could be used for detailed analysis of physical activity practices and whether there are associations. Additionally, South Carolina is a state with a diverse population which will allow us to determine whether there is, in fact, effect modification by race.

2.5 STUDY AIM

The aim of this study is to examine the association between physical activity during pregnancy and infant outcomes (i.e. birthweight and preterm deliveries) among SC women and the possible modifying roles of race/ethnicity and pre-pregnancy BMI status.

Research Question 1. Is physical activity during pregnancy associated with preterm births? Is this relationship modified by race/ethnicity and pre-pregnancy BMI?

Research Question 2. Is physical activity during pregnancy associated with birth weight? Is this relationship modified by race/ethnicity and pre-pregnancy BMI?

I hypothesize that increased physical activity during pregnancy is associated with reduced odds of preterm birth, reduced odds of macrosomia, and reduced odds of large-for-gestational age births. These relationships may be modified by BMI and race.

CHAPTER III

METHODS

3.1 STUDY POPULATION

The Pregnancy Risk Assessment Monitoring System (PRAMS) is a national cross-sectional surveillance system carried out through a collaborative effort between the CDC and state health departments, on a yearly basis. The PRAMS survey randomly samples women who have recently given birth to a live infant in South Carolina, oversampling women who delivered low birth weight (<2500 g) births. Based on information in their newborn's birth certificate roughly 200 mothers are selected to be sampled each month, which is referred to as a "batch", and these mothers are sent paper questionnaires through the mail⁸⁵. A selected woman first receives a pre-letter by mail informing her that she will receive a survey. She will then receive the questionnaire packet by mail several days to a week after receiving the pre-letter. A week later she will receive a "tickler" that serves the purpose of a thank you letter, or a reminder to fill out the survey. Up to two more questionnaires can be sent after this point. If the mothers do not respond to the paper survey an attempt is made to complete the survey by telephone⁸⁵. SC PRAMS oversamples women based on the birthweights of their neonates, including every infant born with a very low birthweight (<1500 grams), 1/6 infants born with moderately low

birthweights (1500-2499g), and about 1/70 women who delivered a child with a normal birth weight ($\geq 2500\text{g}$)⁸⁶. Sampling weights provided in SC PRAMS take into account the complex sample design, non-response, and omissions in the sampling frame in order to be representative of the entire population of pregnant women in South Carolina population⁸⁵.

The questionnaire surveys new mothers on various topics such as access to prenatal care, pre-pregnancy BMI, and health behaviors before and during pregnancy. As the survey population is sampled from recent birth certificate records of live deliveries, data on birth outcomes such as birth weight and gestational age are measured objectively⁸⁶, which makes misclassification of our outcome unlikely.

All data will be obtained from SC PRAMS Phase VI (2009-2011) and Phase VII (2012-2015), which is carried out through a collaborative effort between the CDC and the South Carolina Department of Health and Environmental control. A total of 6391 mothers completed the 2009-2015 SC PRAMS. Their data are weighted to be representative of the roughly 180,000 mothers who gave birth in SC during this period⁸⁵. Our study population consisted of singleton live births, excluding births with gestational age under 23 weeks and gestational birth weight less than 500 grams, born to mothers who did not have pre-existing diabetes. This left us with an initial sample of 5321 mother neonate pairs for our initial analysis.

3.2 PHYSICAL ACTIVITY MEASURES

As with most national surveys, SC PRAMS uses self-reported data rather than objective measurements to assess physical activity. Using information available in SC PRAMS, we assessed physical activity in the following four ways.

PHYSICAL ACTIVITY BEFORE AND DURING PREGNANCY

This study considered a woman being physically active using four primary categories.

- 1) Women who reported being physically active before but not during pregnancy.
- 2) Women who reported being physically active during but not before pregnancy.
- 3) Women who reported being physically active both during and before pregnancy.
- 4) Women who reported being not physically active before or during pregnancy.

The categories where a woman was physically active before pregnancy, during pregnancy, and both before and during pregnancy were compared with the reference group of women who were not physically active at any point. This allowed us to examine whether PA during pregnancy has any impact on birth outcomes after considering a woman's PA before pregnancy.

Physical activity before pregnancy was assessed by the response to the question "Thinking back to 3 months before you found out you were pregnant; did you exercise or play sports at least 3 times a week? (Include walking briskly for ½ hour or more, jogging, aerobics, swimming, etc.) with a response of "yes" or "no". The next question, about physical activity during pregnancy is analogous to the previous but addresses physical activity partaken *during* pregnancy. There are slight changes of wording and options between phase VI and phase VII, and these are detailed in table 3.1. The most pertinent of these changes is that the question about physical activity in phase VII is categorical, rather than dichotomous, asking how many times a week (0,1,2,3,4,5+) a woman exercised. As such, physical activity before and during pregnancy was made dichotomous for both datasets, defining women exercising 3 or more times per week (for at least ½ hours per exercise) as being physically active.

DURATION OF PHYSICAL ACTIVITY DURING PREGNANCY

We examined the dose of physical activity during pregnancy through studying the reported duration in months that a woman was physically active during pregnancy. SC PRAMS asked “How many months of this pregnancy did you exercise or play sports at least 3 times a week?” This was categorized as “0 months” (reference), “1-2 months” of physical activity, 3+ months of physical activity during pregnancy. The reference category also included women who were either not physically active or did not report completing a month of exercise.

TYPE OF PHYSICAL ACTIVITY DURING PREGNANCY

We examined the type of physical activity that a woman undertook during pregnancy, which was broadly categorized as “walking”, “other”, and “none”. There are a broad variety of answers for this specific question. Women who reported walking and who reported other forms of physical activity were compared separately with the reference group of women who were not physically active and reported no type of physical activity.

The sport or exercise most frequently performed, was assessed with the question “What kind of exercise or sport did you do most often during your pregnancy”. Where a woman checked multiple boxes and/or wrote in a response indicating multiple forms of exercise, the woman was coded as having “other” physical activity.

PHYSICAL ACTIVITY INDEX

The three other measures of physical activity were used to make a separate physical activity index (PAI) similar to Liu (2008)⁸⁷. This measure took into account both the duration and intensity of exercises that a woman reported during pregnancy. The

general concept is that women who are physically active during pregnancy were assigned a Metabolic Equivalent of Task (MET) score for their choices of physical activity and this was multiplied by the number of months that they were physically active. We considered women physically active at the 85th percentile of PAI score, 1 standard deviation above the median PAI score, and compared them with those considered inactive, below the 85th percentile. As the questions pertaining to duration of physical activity and type of physical activity only address physical activity during pregnancy, this analysis was limited to women who were physically active during pregnancy compared with a reference group of women who were not.

Within our data set, the duration of physical activity is coded as a continuous variable, and remained that way for the purposes of the model with a few exceptions. Several participants reported being physically active for an unlikely “10 months” (n=5), and an impossible “12 months” (n=4). These will be recoded as 9 months. Where a number of months is not listed, or where the woman was physically inactive, it was coded as 0 months.

To measure the vigor and intensity of physical activity by general type, we used information from the *2011 Compendium of Physical Activity* to determine what MET scores are appropriate⁸⁸. MET is defined as the ratio of work metabolic rate to a standard resting metabolic rate; essentially how many times more energy someone expends during an exercise or activity than in a completely rested state⁸⁸. The *2011 Compendium of Physical Activity* is the most recent method of determining MET and has a variety of types of physical activities classified and sub-classified by description of that activity⁸⁸.

We determined MET scores by the activity that fits the description best, or else determined the mean of the most likely activities given the description.

Several categories of activities were explicitly mentioned by the survey and fit the description in the compendium quite well; brisk walking was categorized with a MET score of 4.3, hiking with a MET score of 6.0, aerobic dancing a MET score of 6.5, cycling a MET score of 8.0, and running/jogging a MET score of 6.0. Most activities required an educated guess on the intensity, using the assumption that the exercise is of light or moderate vigor. While swimming has a wide range of categories ranging from slow water walking (2.5 METS) to fast skin diving (15.8 METS), neither are particularly consistent with what we would consider exercise for the average adult, so we used the midpoint (6.7 METS) between treading water (3.5 METS) and vigorously swimming laps (9.8 METS). “Other dancing” was coded as the midpoint (5.4 METS) between slow ballroom dancing (3.0 METS) and general dancing (7.8 METS). Finally, we coded calisthenics to reflect the midpoint (3.3 METS) of light (2.8 METS) and moderate calisthenics (3.8 METS). Yoga ranges from 2.0 METS (Nadisodhana) and 4.0 METS (power yoga) and was coded as the midpoint (3.0 METS) between these.

There are a wide variety of responses that did not fit the categories well (such as “playing with children” and “crossfit”), and these MET scores are determined on an individual basis using information in the compendium. When a response indicated two or more types of physical activity, the mean of the MET scores were used.

Where a woman claims to have been physically active, but did not specify the type of physical activity, we will assign 3.5 METS, the score for walking at a moderate pace⁸⁸, as this is a more conservative estimator of our most frequently reported category

of physical activity (brisk walking). Where a woman was not physically active, she was assigned 1.0 METS, as it is the baseline MET score. As previously discussed, we created our PAI scores through multiplying the MET scores of the given activity with the duration of the activity in months.

3.3 BIRTH OUTCOMES

Preterm birth was ascertained using a clinical estimate of gestational age found on the birth certificate. While several methods can be used to evaluate gestational age, a National Center for Health Statistics report has found that for stages of preterm birth, there is fair to high sensitivity and high specificity between last menstrual period estimation and clinical estimation of gestational age^{86,89,90}, and, as previously mentioned, is measured by healthcare providers⁸⁶, which reduces our potential for misclassification compared with maternal recall. Our bivariate analysis assessed very preterm births at <34 weeks, moderate preterm births at 34-36 weeks, compared with full term births at >=37 weeks, and our main analysis assesses preterm births <37 weeks compared with full term births⁸⁸.

Low birth weight was ascertained using birth certificate data under 2500g, and macrosomia was defined as births over 4000g, but as birth weight increases with the duration of gestational age this was limited to infants that are not preterm; only infants born after a clinical estimation of gestational age above 37 weeks were assessed for this outcome.

Weight for gestational age was categorized according to the weight distributions for weeks of gestational age by biological sex as described in Kramer (2001), where normal birth ranges for gestational age were derived from three years of all Canadian

births (1994-1996)⁹¹. Infants with a birth weight less than the 10th percentile or greater than the 90th percentile for their clinical gestational age are considered, respectively, small for gestational age and large for gestational age. All births provided in the SC PRAMS are included in this outcome.

3.4 COVARIATES

The covariates included in the initial model are derived from covariates in the literature for preterm birth and birth weight outcomes. Our analyses for both preterm birth and gestational age for all adjusted models included maternal age (categorical), insurance type (medicaid/private/self-pay) and parity (first birth, second or more). Variables that were assessed for inclusion into the model included smoking (yes/no), gestational weight gain (below recommendations, within recommendations, above recommendations, for BMI category), education (<high school, high school, some college or higher), pregnancy intention (trying, did not want, was not trying), and infant sex (male/female). We also adjusted for pregnancy risk factors (pre-pregnancy or gestational diabetes, pre-pregnancy or gestational hypertension, eclampsia, previous risky pregnancy outcomes, and/or, previous caesarian compared with women who did not have these risk factors).

A separate model was created that excluded women with pre-pregnancy or gestational hypertension from the sample. We know from Gruendelman (2013) that there may be effect modification between physical activity and preterm delivery by pre-pregnancy BMI (below 25BMI/at or above 25BMI) and, as suggested in the literature discussion section of this paper, race (white/ black or other), may also be an effect

modifier for physical activity on birth outcomes, but literature examining this is sparse. Effect modification by these variables was assessed within the main analysis.

3.5 STATISTICAL ANALYSIS

Our sample population was initially described in terms of the women's demographic, health, and socioeconomic characteristics. We also examined women's physical activity habits in depth, and neonatal outcomes within our sample.

Contingency tables and the chi-square statistic were used to examine bivariate differences in sample demographics and birth outcomes by physical activity status, both before and during pregnancy (modeled as YN, NY, YY, NN). Crude and adjusted logistic regression were used to determine the association between physical activity and birth outcomes. The adjusted model was determined a priori for each outcome and then fit using backward selection if the analysis of effect was below $p=0.15$.

As discussed earlier, our independent variables were measured in four ways. For each of our outcomes four different PA measures were included into the models one at a time. We also will be using a PAI as described in the methods section. These will be used to assess the association of PA with preterm birth, size for gestational age (reference appropriate weight range for GA⁹¹), and birth weight outcomes including macrosomia and low birth weight (reference normal BW) in the overall population. Additionally, where effect modification by race or BMI is observed, we will stratify by race or pre-pregnancy BMI.

A total of 6391 women participated in PRAMS between 2009 and 2015. We excluded women who did not have singleton births ($n=624$), women who delivered an infant under 500g ($n=234$), women who delivered a live birth prior to 22 weeks of

age(n=6), and women with preexisting diabetes(n=213). This left us with a sample of 5321 mother-neonate pairs. For our main analysis, we also removed all missing responses for our chosen covariates, leaving us with 5294 mother-neonate pairs.

Some of the write in questions on the survey provided responses that were inconsistent with the other answers the respondent had chosen, notably 10 women had written in that they had completed no exercise during pregnancy despite that some had previously answered that they were physically active during pregnancy. These women were recoded as physically inactive, and their type of physical activity was recoded as “missing”.

Other women had write-in responses about their type of physical activity that were inconsistent with their categorical responses; for example, a woman may have selected “other exercise” and written in “walking” instead of choosing “brisk walking”. Because of this, 22 women were re-categorized as having walking as their main exercise, 4 were reclassified as having participated in calisthenics/general exercise, one was reclassified as jogging/running, and 9 women from phase 6 were reclassified as having partaken in yoga, to be consistent with the yoga category added in phase 7. A large number of physically active participants (n=188) selected or wrote in more than one type of physical activity when only one type was requested or else chose a category; these were all coded as “other” exercise.

Database management and statistical analysis were carried out using SAS software version 9.4 (SAS Institute, Cary, NC). All results were weighted to be representative of all live births from 2009-2015 in South Carolina and were considered significant at $p \leq 0.05$.

Table 3.1: Wording of Questions and Responses Between SC PRAMS Phases

Question	Wording of Question Phase 6	Wording of Question Phase 7	Responses Phase 6	Responses Phase 7
<i>LTPA Before Pregnancy</i>	Thinking back to 3 months before you found out you were pregnant, did you exercise or play sports at least 3 times a week?	Thinking back to 3 months before you found out you were pregnant, how many times did you exercise or play sports per week?	Yes/No	0 times 1 time 2 times 3 times 4 times 5 or more times
<i>LTPA During Pregnancy</i>	Thinking back to after you found out you were pregnant, did you exercise or play sports at least 3 times a week?	Thinking back to after you found out you were pregnant, how many times did you exercise or play sports per week?	Yes/No	0 times 1 time 2 times 3 times 4 times 5 or more times
<i>Duration of LTPA during pregnancy</i>	How many months of this pregnancy did you exercise or play sports at least 3 times a week?	During how many months of this pregnancy did you exercise or play sports at least 3 times a week?	__ Months	__ Months
<i>Type of LTPA preferred</i>	What kind of exercise or sport did you do most often during your pregnancy?	What kind of exercise or sport did you do most often during your pregnancy?	Brisk walking Hiking Jogging or running Aerobics or aerobic dancing Other dancing Calisthenics or general exercise Biking Swimming or water exercise Other	Brisk walking Hiking Jogging or running Aerobics or aerobic dancing Other dancing Calisthenics or general exercise Biking Swimming or water exercise Yoga or pilates Other

CHAPTER IV

RESULTS

4.1 SAMPLE CHARACTERISTICS

Table 4.1 summarizes some of the weighted sample characteristics of our population. Our sample was predominantly white women (60.9%), 20-29 years old (55%), with college education(57.8%), whose pregnancies were unplanned (57.7%). Most of these women did not smoke (88.6%), did not have a history of high blood pressure 92.1%, and the majority had gestational weight gain higher than the Institute of Medicine's recommendations (47.1%). The physical activity traits of the sample population are detailed in table 4.2. About 45.8% of women in our sample reported being physically active prior to pregnancy, but only 32.5% reported being active during pregnancy. A large proportion were not physically active at any point; 48.6% of women reported not being physically active prior to or during pregnancy whereas 26.9.0% reported being physically active both before and during their pregnancy. The rest reported either being physically active before, but not during, pregnancy (18.9%), or during pregnancy, but not before (5.5%). As for the duration of physical activity, 70% of women reported less than 1-month of physical activity during pregnancy while 27.1% of women in our sample reported being physically active for three or more months of pregnancy.

Brisk walking was the most popular activity among women who were physically active during pregnancy; 63.5% of women reported brisk walking as their primary means of exercise. Other categories included jogging/running (4.3%) and yoga (2.2%). Twenty percent of women wrote in an unlisted category or selected more than one category (data not shown).

Our outcomes are provided in table 4.3. A majority of babies (91.5%) were delivered full term, with the moderately (34-36 weeks) preterm (6.2%) or very (<34 weeks) preterm (2.2%). In our weighted sample, 84.6% of women had infants within normal ranges for birth weight (2500-3999g), whereas 7.6% had infants with low birth weight, and 7.8% had infants with macrosomia. When being compared to the standard reference population, 77.7% of women having infants whose birthweight was appropriate for their gestational age at birth, with 12% being small for gestational age, and 10.3% being large for gestational age.

4.2 BIVARIATE ANALYSIS

The results of our bivariate analysis for our demographics is displayed in table 4.4. Most notable is that women who were physically active before and during pregnancy, as well as women who were active before, but not during pregnancy, were more likely to be well educated, white, normal pre-pregnancy weight, first time parents, non-smokers and had intended pregnancies compared with women who were not physically active before or during their pregnancy.

The results of bivariate analysis for our exposure categories and outcomes is displayed in table 4.5. Women who were physically active during pregnancy (4.0% (95% CI, 1.1-6.7), but not before pregnancy, and women who were physically active before and

during pregnancy (4.9% (95% CI, 3.5-6.3%)) had significantly higher prevalence of preterm birth ($p=0.0069$) preterm infants than women who exercised before, but not during pregnancy (8.4% (95% CI, 5.9-10.9%)). The patterns of associations for weight for gestational age and birth weight were less clear, with women active before pregnancy, but inactive during pregnancy having the highest prevalence of delivering LGA (14.6% (95% CI, 10.9-18.4%)) and macrosomic infants (10.7% (95% CI, 7.4-14.0%)), and women active during, but not before pregnancy having the highest prevalence of SGA infants (11.9% (95% CI, 9.2-14.6%)).

4.3 MAIN ANALYSIS

We conducted our main analysis using multinomial logistic regression models between physical activity exposures and preterm birth, birth weight, and size for gestational age. We also utilized a separate model that excluded individuals with pre-existing or gestational hypertension for the purpose of a sensitivity analysis as to the role of hypertension in the association. Effect modification by race or BMI was not observed with a significant effect for any analysis.

Women who were physically active during pregnancy at all, regardless of their physical activity before pregnancy had significantly lower crude odds of preterm birth (OR=0.69 (95% CI, 0.53, 0.89)) and lower crude odds of delivering low birth weight infants (OR=0.82 (95% CI, 0.71, 0.96)) than women who were not (data not shown). The strength of these results attenuated after adjustment adjusting for smoking, maternal education, maternal age, maternal race, maternal risk factors, insurance and gestational weight gain and BMI but remained significant for preterm birth (aOR= 0.70 (95% CI,

0.53-0.91)) and low birth weight (aOR 0.84 (0.70-0.99)(data not shown). No association between physical activity before birth as a whole and any birth outcome was found.

PRETERM BIRTH

When examining the periods in which a woman was physically active during and before pregnancy, there were variety of significant results for preterm birth, the findings of which are displayed in table 4.6. Women who were physically active during, but not before pregnancy had significantly reduced odds of preterm birth after adjustment (aOR=0.54 (95% CI, 0.30-0.98)) compared with inactive women. Using the PAI model, women considered to be highly physically active (>85th percentile PAI score) had significantly reduced odds of preterm births (OR=0.64 (0.46-0.89)) compared with women who were under this threshold. The odds of preterm birth continued to be significantly reduced in this population after adjustment (aOR=0.69 (0.49-0.96)). Women who stopped physical activity around the time when they became pregnant, conversely had significantly higher risk (aOR=1.50 (95% CI, 1.07-2.10)) compared with inactive women.

We also examined how the type of physical activity and duration of physical activity affected risk of preterm birth. While brisk walking was associated with reduced point estimates for preterm birth compared with no exercise, this did not reach significance. The category of other types of physical activity was significantly associated with reduced odds of preterm birth (OR= 0.60 (95% CI 0.42-0.87)). This relationship remained significant (aOR= 0.63 (95% CI 0.43-0.91)) after adjusting for smoking, maternal education, maternal age, maternal race, maternal risk factors, insurance and gestational weight gain and BMI. Compared with women who engaged in no physical

activity, women engaged in 3-9 months of physical activity had significantly reduced risk of preterm birth (OR=0.70 (95% CI, 0.53-0.93)). After adjusting for smoking, maternal education, maternal age, maternal race, maternal risk factors, insurance, BMI, and gestational weight gain, this relationship also remained significant (aOR= 0.72 (95% CI, 0.54-0.97)). In the model where women with pre-existing hypertension were removed, only women who exercised with an activity other than brisk walking had a significant reduction in odds of preterm birth after adjustment (aOR= 0.62 (95% CI, 0.41-0.94)) compared with inactive women. Women who were active prior to pregnancy but stopped during pregnancy also continued to have significantly higher odds of preterm birth (aOR= 1.54 (95% CI, 1.06-2.25)) compared with inactive women in this model.

LOW BIRTH WEIGHT AND MACROSOMIA

The outcomes of macrosomia and low birth weight were examined using multinomial logistic regression and the findings are presented in table 4.7. The direction of the effects by category was generally similar to preterm birth. For women physically active before, but not during pregnancy, odds of macrosomia were significantly elevated in the crude model (OR=1.58 (95% CI, 1.02-2.45)) but attenuated and lost significance after adjusting for maternal age, maternal education, maternal race, maternal risk factors, insurance, BMI, and gestational weight gain. While the odds of low birth weight deliveries were not significantly elevated in the crude model, after adjusting for the same factors, we found 33% increased odds of low birth weight (aOR= 1.30 (95% CI, 1.03-1.62)).

Significant odds reductions were observed for low birth deliveries in the crude model among women who were physically active before and during pregnancy (OR=0.82

(95% CI, 0.69-0.96)) for macrosomia in the PAI model (OR=0.75 (95% CI, 0.61-0.92) and for LBW among women who reported 3 or more months of exercise (OR=0.83 (95% CI, 0.70-0.98)), but these associations lost significance in the adjusted models. No other significant findings were observed. In the model where women with pre-existing hypertension were removed, point estimates for adjusted odds of macrosomia and low birth weight changed slightly but no results reached significance.

WEIGHT BY GESTATIONAL AGE

The results for weight for gestational age are displayed in table 4.8. Odds of LGA birth were elevated among women who were physically active before, but not during pregnancy in the crude model (OR=1.61 (95% CI, 1.11-2.35)) and remained significant (aOR= 1.59 (95% CI, 1.08-2.34)) after adjusting for maternal age, maternal education, maternal race, maternal risk factors, insurance and gestational weight gain. Point estimates for other exercise and months of exercise generally suggested reduced risk of LGA, but no significant reduction (or increase) in odds for these exposures was observed. In the model where women with pre-existing hypertension were removed, women who were physically active prior to pregnancy but not during pregnancy, remained at higher adjusted odds of LGA (aOR= 1.61 (95% CI, 1.07-2.42)) than women who were inactive, but no other significant findings were noted.

Table 4.1 Sample Characteristics of SC Women Who Recently Delivered Live Births

Characteristic	N.	Weighted Percent
Education		
<i>Below High School</i>	881	17.8%
<i>High School diploma</i>	1274	24.5%
<i>College</i>	3139	57.8%
Maternal Age		
<i>Under 20</i>	527	10.8%
<i>20-29 years</i>	2851	55.0%
<i>30+ years</i>	1916	34.2%
Ethnicity		
<i>White</i>	2810	60.9%
<i>Black</i>	2027	30.3%
<i>Other</i>	457	8.8%
Pre-pregnancy Weight		
<i>Underweight</i>	574	9.8%
<i>Normal Weight</i>	2139	42.2%
<i>Overweight</i>	1157	22.4%
<i>Obese</i>	1424	25.6%
Smoking Status		
<i>Non-Smoker</i>	4612	88.6%
<i>Smoker</i>	678	11.4%
History of High Blood Pressure		
<i>Yes</i>	945	7.9%
<i>No</i>	4349	92.1%
Pregnancy Intention		
<i>Unintended</i>	3033	57.7%
<i>Intended</i>	2073	42.3%
Gestational Weight Gain^a		
<i>Below IOM Recommendation</i>	2195	28.0%
<i>IOM Recommended</i>	1212	24.9%
<i>Above IOM Recommendations</i>	1887	47.1%
Parity		
<i>First Child</i>	2494	40.9%
<i>Second or greater Child</i>	2691	59.1%
^a Based on IOM guidelines		

Table 4.2 PA Among SC Women Who Recently Delivered Live Births

Characteristics	N.	Weighted Percent
<i>Exercise 3 times a week 3 months Before Pregnancy</i>		
Yes	2339	45.8%
No	2960	54.2%
<i>Exercise 3 times a week During Pregnancy</i>		
Yes	1541	32.5%
No	3748	67.5%
<i>Exercise Status before and during Pregnancy</i>		
Not Active	2712	48.7%
Active Before, Not During	1022	18.9%
Active During, Not Before	235	5.5%
Active Before & During	1298	26.9.0%
<i>Months of Physical Activity During Pregnancy</i>		
0 months	3871	71.1%
1-2 month	188	2.8%
3+ months	1213	26.1%
<i>Type of Physical Activity Reported</i>		
Brisk Walking	822	52.9%
Other	706	47.1%

Table 4.3 Descriptive Statistics of Infants Born to SC Women

Characteristics	N.	Weighted Percent
<i>Biological Sex</i>		
Male	2613	49.0%
Female	2681	51.0%
<i>Gestational Age at Delivery</i>		
Normal term	2406	91.5%
Moderately Preterm ^a	689	6.2%
Very Preterm ^b	2199	2.2%
<i>Weight for gestational age^c</i>		
Small for Gestational Age	1407	11.9%
Appropriate for Gestational Age	3556	77.7%
Large for Gestational Age	336	10.4%
<i>Birth Weight</i>		
Low Birth Weight ^d	3412	7.6%
Normal Birth Weight	1718	84.6%
Macrosomia ^d	164	7.8%
^a Defined as gestational age at birth between 36 and 34 weeks ^b Defined as gestational age at birth below 34 weeks ^c Defined as <10 percentile for SGA and >90 percentile for LGA as defined in Kramer 2001 ^d macrosomia defined as delivery birth weight ≥3999g, lbw defined as delivery birth weight at ≤2500 g		

Table 4.4 Characteristics of SC Women by PA During Pregnancy

	<i>Active Only Before Pregnancy</i>		<i>Active Only During Pregnancy</i>		<i>Active before and during Pregnancy</i>		<i>Not Active Before or During Pregnancy</i>		<i>X²-Value</i>
	n.	Weighted %	n.	Weighted %	n	Weighted %	n.	Weighted %	
<i>Education</i>									
<i>Below HS</i>	124	13.5%	55	23.5%	217	16.8%	473	18.8%	P<0.001
<i>HS diploma</i>	216	14.1%	55	22.7%	253	19.0%	742	28.9%	
<i>College</i>	682	64.6%	125	53.8%	828	64.2%	1497	52.3%	
<i>Race</i>									
<i>White</i>	573	68.2%	102	44.9%	793	67.9%	1341	56.3%	P<0.001
<i>Black</i>	374	26.4%	113	42.5%	392	24.7%	1141	33.6%	
<i>Other</i>	79	5.4%	21	12.6%	119	7.5%	235	10.1%	
<i>BMI Status</i>									
<i>Underweight</i>	87	7.6%	23	10.7%	147	10.6%	312	10.0%	P<0.001
<i>Normal Weight</i>	412	44.4%	93	34.3%	628	49.1%	1003	38.4%	
<i>Overweight</i>	259	25.4%	55	28.3%	267	21.3%	574	21.3%	
<i>Obese</i>	269	22.6%	65	26.7%	262	19.0%	828	30.3	
<i>Smoking</i>									
<i>Non-Smoker</i>	932	92.9%	204	90.3%	1143	90.1%	2309	85.9%	P=0.0018
<i>Smoker</i>	88	7.1%	31	9.7%	154	9.9%	402	14.1%	
<i>Pregnancy Intention</i>									
<i>Not intended</i>	554	55.3%	152	65.5%	685	52.1%	1639	60.8%	P=0.0049
<i>Intended</i>	439	44.7%	79	35.5%)	568	47.9%	983	39.2%	

Table 4.5 Birth Outcomes of SC Women by PA During Pregnancy

	<i>Active Only Before Pregnancy</i>		<i>Active Only During Pregnancy</i>		<i>Active before and during Pregnancy</i>		<i>Not Active Before or During Pregnancy</i>		<i>X²-Value</i>
	n.	Weighted %	n.	Weighted %	n.	Weighted %	n.	Weighted %	
<i>Preterm Status</i>									P=0.0069
<i>Normal term</i>	451	89.3%	129	94.5%	661	93.1%	1157	91.1%	
<i>Preterm^a</i>	149	8.4%	28	4.0%	833	4.9%	326	6.4%	
<i>Very Preterm^b</i>	427	2.2%	79	1.5%	460	2.0%	1234	2.5%	
<i>Weight for GA</i>									P=0.1157
<i>Small for GA</i>	274	10.8%	63	14.1%	332	11.9%	730	12.3%	
<i>Average GA</i>	684	74.6%	154	75.0%	886	79.3%	1827	78.2%	
<i>Large for GA</i>	69	14.6%	19	10.9%	86	8.8%	160	9.5%	
<i>Birth Weight</i>									P=0.1423
<i>Normal Weight</i>	316	81.5%	93	86.0%	498	86.0%	806	84.8%	
<i>Macrosomia</i>	41	10.7%	7	7.1%	44	7.2%	71	7.0%	
<i>Low Birth Weight</i>	670	7.8%	136	6.9%	762	6.7%	1840	8.1%	

Table 4.6 Logistic Regression Between Maternal PA and Preterm Birth

	<i>Crude OR of Preterm^a</i>	<i>Adjusted OR^b of Preterm^a</i>	<i>HBP Adjusted OR^f of Preterm^a</i>
<i>PA^c and Pregnancy</i>	OR, 95% CI	aOR, 95% CI	aOR, 95% CI
<i>Not Active</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active Before Pregnancy</i>	1.22 (0.89-1.68)	1.50 (1.07-2.10)	1.54 (1.06-2.25)
<i>Active During Pregnancy</i>	0.61 (0.34-1.08)	0.54 (0.30-0.98)	0.54 (0.27-1.08)
<i>Active Before and During Pregnancy</i>	0.76 (0.57-1.01)	0.83 (0.62-1.12)	0.83 (0.59-1.16)
<i>PAI Model^d</i>			
<i>Lower Activity</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active</i>	0.64 (0.46-0.89)	0.69 (0.49-0.96)	0.70 (0.49-1.02)
<i>Type of Exercise</i>			
<i>None</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Brisk Walking</i>	0.77 (0.56-1.06)	0.75 (0.54-1.04)	0.75 (0.54-1.04)
<i>Other^e</i>	0.60 (0.42-0.87)	0.63 (0.43-0.91)	0.62 (0.41-0.94)
<i>Months of Exercise</i>			
<i>Less than 1 Month</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>1-2 Months</i>	0.98 (0.52-1.86)	0.95 ((0.51-1.78)	0.93 ((0.44-1.95)
<i>3+ Months</i>	0.70 (0.53-0.93)	0.72 (0.54-0.97)	0.74 (0.53-1.03)
<p>^a defined as a live birth with a clinical estimated gestational age of under 37 weeks. ^b adjusted for smoking,maternal education, maternal age, maternal race, maternal risk factors and gestational weight gain, insurance/payment method and BMI ^c Defined as exercise 3x a week 30 minutes a day ^d Active defined as the 85th percentile of PAI Score during pregnancy based on METS by Type of Activity and Duration of Activity ^e Includes other types of exercise and multiple exercises ^f Excludes women with pre-existing or gestational hypertension from sample, adjusted for the same factors</p>			

Table 4.7 Multinomial Regression Between Maternal PA and Macrosomia/LBW

	<i>Crude OR of LBW</i>	<i>Adjusted OR of LBW</i>	<i>Adjusted OR of LBW</i>	<i>Crude OR of Macrosomia</i>	<i>Adjusted OR of Macrosomia</i>	<i>HBP Adjusted OR of Macrosomia</i>
	OR, 95% CI	aOR, 95% CI	aOR, 95% CI	OR, 95% CI	aOR, 95% CI	aOR, 95% CI
<i>PA and Pregnancy</i>						
<i>Not Active</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active Before Pregnancy</i>	0.99 (0.82-1.20)	1.30 (1.03-1.62)	1.20 (0.94-1.53)	1.58 (1.02-2.45)	1.43 (0.91-2.26)	1.37(0.86-2.17)
<i>Active During Pregnancy</i>	0.84 (0.60-1.18)	0.72 (0.49-1.08)	0.70 (0.45-1.07)	1.01 (0.41-2.51)	1.01 (0.43-2.39)	1.11(0.47-2.62)
<i>Active Before and During Pregnancy</i>	0.82 (0.69-0.97)	0.96 (0.79-1.18)	0.93(0.75-1.16)	1.02 (0.67-1.56)	1.04 (0.68-1.60)	0.95(0.60-1.49)
<i>PAI Model</i>						
<i>Lower Activity</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active</i>	0.75 (0.62-0.90)	0.85 (0.69-1.06)	0.87(0.69-1.08)	0.79(0.50-1.26)	0.81 (0.51-1.29)	0.76(0.46-1.25)
<i>Type of Exercise</i>						
<i>None</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Brisk Walking</i>	0.89 (0.73-1.07)	0.87 (0.69-1.09)	0.86 (0.67-1.10)	0.96 (0.59-1.54)	0.97 (0.60-1.57)	0.93 (0.56-1.55)
<i>Other</i>	0.75 (0.61-0.92)	0.84 (0.66-1.07)	0.82 (0.63-1.05)	0.80 (0.49-1.32)	0.85 (0.51-1.41)	0.79 (0.47-1.35)
<i>Months of Exercise</i>						
<i>Less than 1 Month</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>1-2 Months</i>	1.08 (0.72-1.62)	1.14 (0.43-1.79)	1.12(0.69-1.81)	1.17 (0.48-2.87)	1.09 (0.43-2.77)	1.20(0.47-3.08)
<i>3+ Months</i>	0.83 (0.70-0.98)	0.91 (0.54-1.01)	0.91(0.74-1.12)	0.81 (0.53-1.22)	0.82 (0.72-1.79)	0.75(0.47-1.17)

Table 4.8 Multinomial Regression Between Maternal PA and Birthweight

	<i>Crude OR of SGA</i>	<i>Adjusted OR of SGA</i>	<i>Adjusted OR of SGA</i>	<i>Crude OR of LGA</i>	<i>Adjusted OR of LGA</i>	<i>HBP Adjusted OR of LGA</i>
<i>PA and Pregnancy</i>	OR, 95% CI	aOR, 95% CI	aOR, 95% CI	OR, 95% CI	aOR, 95% CI	aOR, 95% CI
<i>Not Active</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active Before Pregnancy</i>	0.92 (0.65-1.31)	1.17(0.80-1.71)	1.13 (0.74-1.70)	1.61 (1.11-2.35)	1.59 (1.08-2.34)	1.61(1.07-2.42)
<i>Active During Pregnancy</i>	1.21 (0.71-2.08)	1.12 (0.63-1.97)	1.21 (0.66-2.20)	1.20 (0.59-2.47)	1.19 (0.59-2.40)	1.20(0.58-2.47)
<i>Active Before and During Pregnancy</i>	0.94 (0.69-1.29)	1.08 (0.78-1.50)	1.08(0.76-1.52)	0.92 (0.63-1.33)	0.98 (0.67-1.43)	0.93(0.62-1.39)
<i>PAI Model</i>						
<i>Lower Activity</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Active</i>	0.91 (0.62-1.34)	1.27 (0.91-1.77)	1.29(0.91-1.83)	1.08 (0.78-1.49)	0.96 (0.65-1.44)	0.90(0.59-1.38)
<i>Type of Exercise</i>						
<i>None</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>Brisk Walking</i>	1.02(0.72-1.46)	1.06 (0.74-1.51)	1.05 (0.71-1.55)	0.97(0.65-1.46)	0.99 (0.66-1.48)	0.93 (0.60-1.42)
<i>Other</i>	1.00 (0.65-1.46)	1.15 (0.66-1.48)	1.20(0.80-1.78)	0.68 (0.43-1.06)	0.88 (0.70-1.10)	0.73 (0.44-1.18)
<i>Months of Exercise</i>						
<i>Less than 1 Month</i>	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
<i>1-2 Months</i>	0.42 (0.16-1.11)	0.45 (0.16-1.25)	0.46(0.15-1.44)	1.03 (0.45-2.35)	0.99 (0.44-2.26)	1.17(0.52-2.66)
<i>3+ Months</i>	1.13 (0.85-1.51)	1.28 (0.44-2.26)	1.30(0.95-1.78)	0.81 (0.57-1.16)	0.84 (0.58-1.21)	0.76(0.51-1.13)

CHAPTER V

DISCUSSION AND CONCLUSIONS

5.1 DISCUSSION

We used a large, ethnically diverse sample population weighted to be representative of the population of SC, and found that physical activity during pregnancy was associated with significantly reduced risk of preterm birth compared with women who were not physically active; this effect was particularly noteworthy in previously inactive women who started physical activity during pregnancy, who had 46% reduced risk compared with inactive women. Our results indicated a dose response as well; women who reported 3-9 months of physical activity had a significant 28% decrease in odds of preterm birth compared with women who reported less than one month after adjusting for confounders whereas women who reported 1-2 months had only a point estimate indicative of a 5% decrease compared with women who reported less than one month. Furthermore, we found while women who walked had odds ratios indicative of a 25% decrease in preterm birth, this was not significantly higher than women who did no exercise, but women who reported exercise other than walking or more than one exercise had a significant 37% decrease in preterm birth compared with women who did none. We also found that women in or above the 85th percentile of physical activity score had 39%

decreased risk compared with women below the 85th percentile. Overall for preterm birth, physical activity during pregnancy was associated with reduced risk, and our findings for previously inactive women suggest that there may be substantial benefits for preterm birth even at a fairly low physical activity threshold. No significant protective effects were observed for low birth weight, macrosomia, small for gestational age, and large for gestational age births in the adjusted models.

Previously active women who stopped physical activity prior to pregnancy conversely had adverse outcome; 51% increased odds of preterm birth, 30% increase in LBW and 59% increase in LGA after adjustment for maternal age, maternal education, maternal race, maternal risk factors, insurance, BMI, and gestational weight gain compared with inactive women.

While no study included in our literature review conceptualized physical activity using the same methods of classifying exposure, we found that our findings for physical activity during pregnancy and preterm birth were generally consistent with the literature found in Kahn³⁴.

We did not find a significant benefit of physical activity during pregnancy on birth weight or size for gestational age outcomes, which was somewhat inconsistent with our expectations given the literature reviewed in Bisson. It was unexpected to find significantly increased odds for adverse preterm outcomes, birth weight, and size for gestational among women who were physically active prior to pregnancy but did not continue to be during pregnancy compared with women who were never active. It seems unlikely that physical activity prior to pregnancy in of itself would result in adverse birth outcomes, and women who were sedentary during pregnancy should not be so different

from women who were not physically active during the study. It seems most likely that the change in risk is related to the cessation of physical activity before pregnancy; either the factor that caused a mother to stop exercising, or the change from a physically active to a sedentary lifestyle. We attempted to control for risk factors, such as previous preterm births, gestational hypertension, and gestational diabetes, using birth certificate data, but this did not change the significance of the association.

The dataset for our study was fairly large and was weighted to be representative of the population of the state, allowing for externally valid conclusions. We used multiple measures of physical activity during pregnancy especially the perinatal patterns of physical activity, which allow us to more thoroughly examine the associations of interest and thus contribute new information to the existing literature on this subject. Only four studies we reviewed^{44,46,80,82} attempted to address the impact of physical activity prior to pregnancy and generally found no differences or else found beneficial effects, whereas we found no aggregate benefit to pre-pregnancy leisure-time physical activity and detriment in women who were previously physically active, but stopped when they became pregnant. Several studies examined the period during pregnancy in which a woman was physically active and generally found benefits or no effect. Our study found no significant aggregate effect of preterm exercise on our outcomes, but ours is the first, to our knowledge, that examines women who ceased physical activity after becoming pregnant and women who were inactive before, but became physically active during pregnancy.

Effect modification was examined for several exposures and outcomes, particularly for race, but none of these were significant in our study. This does not

contradict the findings from Kosa which found significant effect modification deviating in both directions starting at or above 24 BMI⁵² as our dataset included BMI categories, but not numbers, so we were unable to replicate those findings.

Several limitations should be noted. While data on our outcomes was objectively measured, our exposure was self-reported months after a woman had delivered a live birth, which opens up the possibility of recall bias based on the birth outcomes. Second, this may also be prone to social desirability bias, a reporting bias caused by societal values put on certain behaviors in pregnancy. Additionally, we had very little information on the overall distribution of exercise in a given week as we had to dichotomize this information provided in phase 7 to have better consistency with phase 6. It's also not clear how long any individual exercise session was beyond the specification that it was over 30 minutes a day, so it is possible that women exceeded the recommendations for physical activity with two days of vigorous LTPA but were not considered physically active in our sample as they were not active for three days.

There were also issues with the responses for type of physical activity, as the questionnaire asked for one type of physical activity and a number of women chose more than one activity, a woman who wrote that she walked as a hobby and worked a physically demanding job at a hospital would be coded as "other exercise" in our model, and the MET scores for multiple categories were made into a mean score, as if every type of exercise was conducted equally so this should be taken into consideration when interpreting our results for the PAI model.

We were also limited in our ability to assess months of physical activity in detail beyond the number of months that the woman stated she was active, which could be a

problem as the benefit of physical activity during pregnancy may only occur in a specific trimester. We also lacked information on physical disability among women in this study which may be causally related to an inability to exercise and higher risk of birth outcomes. There was also not sufficient information on why women started or stopped physical activity upon becoming pregnant, it is possible that either prescribed bedrest or recommended exercise could lead to these behaviors.

In spite of these potential limitations, our measures of physical activity identified women who exercised routinely (≥ 3 times per week) and who were more physically active than general population and found benefits at a low threshold and generally found increasing benefits with increasing months and vigor. This supports that our findings on PTB are consistent with our hypotheses.

Further and more detailed studies are recommended to confirm the findings on cessation of physical activity upon becoming pregnant, as well as addressing some of the questions that this study was not able to answer adequately due to limitations in survey data.

5.2 CONCLUSIONS

Our results generally suggest that women who exercise during pregnancy, particularly previously inactive women, have significantly lower risk of preterm birth. The hypothesis that women who exercised before pregnancy would also have lower odds of adverse birth outcomes was not supported by our data. Women who were physically active prior to pregnancy but stopped being physically active during pregnancy had significantly higher odds of detrimental outcomes, though this increased risk seems more likely to be from inadequately control for risk factors that would lead to the cessation of

physical activity while pregnant. The results support the general guidelines of the American College of Obstetricians and Gynecologists (ACOG), which state that physical activity during pregnancy is considered to be safe and beneficial for healthy women. We recommend that women be involved with moderate intensity physical activity during their pregnancy, and that women who are physically active, and who are not contraindicated from doing so during pregnancy, continue to be physically active during pregnancy.

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