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DIABETES RISK STATUS AND PHYSICAL ACTIVITY IN PREGNANT WOMEN: U.S. BRFSS 2011, 2013, 2015, 2017.

by

Bethany Grace Rand

A thesis submitted to the Department of Clinical & Applied Movement Sciences in partial fulfillment of the requirements for the degree of Master of Science in Exercise Science and Chronic Disease

UNIVERSITY OF NORTH FLORIDA

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Dedication & Acknowledgements

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Chapter 4: Manuscript

1. Trends in Prevalence of Overt Diabetes and High-Risk for Overt Diabetes in

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Nomenclature

cm	Centimeter	
d/wk	Days per week	
g	Gram(s)	
h	Hour	
kg/m2	Kilograms per meter squared	
MET·min·wk-1	MET minutes per week	
min	Minute	
min/wk	Minutes per week	
mg/dl	Milligrams per deciliter	
mmol/L	Millimoles per liter	

List of Abbreviations

AA	Aerobic activity
A1C	Glycohemoglobin
ACOG	American College of Obstetricians and Gynecologists
ADA	American Diabetes Association
BMI	Body mass index
BRFSS	Behavioral risk factor surveillance system
CI	Confidence interval
CRP	C-reactive protein
CVD	Cardiovascular disease
DHHS	Department of Health and Human Services
DIP	Diabetes in pregnancy
DRS	Diabetic risk factor
E2	Estradiol
GDM	Gestational diabetes mellitus
НАРО	Hyperglycemia and adverse pregnancy outcomes
HBM	Health belief model
hGDM	History of gestational diabetes
hPGH	Human placental growth hormone
hPL	Human placental lactogen
HRD	High risk for diabetes
HS	High school
IADPSG	The International Association of Diabetes Pregnancy Study Groups

IL-6	Interleukin 6
IRS-1	Insulin receptor substrate - 1
LMIC	Low- and middle-income countries
LPS	Liposaccharides
LTPA	Leisure-time physical activity
MIDUS	Midlife in the united states
MSA	Muscle strengthening activity
NHANES	National Health and Nutrition Examination Survey
OGTT	Oral Glucose Tolerance Test
OR	Odds ratio
PA	Physical activity
PD	Pre-diabetes
PG	Plasma glucose
Pg	Progesterone
PGDM	Pre-gestational diabetes
RCT	Randomized controlled trial
SES	Socioeconomic status
STB	Standardized Beta Coefficient
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TNF-α	Tumor necrosis factor- alpha
U.S.	United States
WHO	World health organization

ABSTRACT

- *Objectives* We sought to examine differences in aerobic activity (AA) and muscle strengthening activity (MSA) by diabetes risk status (DRS) among pregnant women in the United States.
- **Background** Pregnant women without complications are advised to engage in physical activity (PA) to mitigate adverse outcomes. Differences may exist among pregnant women of diverging diabetes status in meeting national PA recommendations.
- Methods The sample (n=9,597) included pregnant women ages 18-44, who participated in the 2011, 2013, 2015, and 2017 Behavioral Risk Factor Surveillance System. Levels of DRS were: no diabetes (ND), high risk for diabetes (HRD) due to self-reported gestational diabetes or pre-diabetes, and overt diabetes (DM). Odds ratios (ORs) for meeting PA recommendations were obtained. Covariates included age, race, education, household child count, alcohol consumption, and smoking status.
- *Results* Findings revealed that on average, group DM had 46.5 fewer minutes of weekly AA compared to group ND. Furthermore, a significantly lower OR (0.39; P<0.05) for meeting both recommendations in group DM (referent ND) was observed after adjustment.
- *Conclusions* We observed pregnant women with overt diabetes have a lower likelihood of engaging in PA, while group HRD was similar in their PA engagement as group ND. Solutions should be explored for improving PA participation in

pregnant women with diabetes so that they may also enjoy the health benefits. Actions include increasing PA promotion by clinical providers, implementing methods for overcoming barriers to PA, and exploring strategies to make exercise palatable to this population. **Chapter 1: Introduction**

BACKGROUND

Hyperglycemia refers to the presence of glucose in the blood, above the normal range (1). In pregnancy, hormone changes lead to attenuated insulin sensitivity (2-4). As a result of impaired glucose uptake in healthy pregnant women, excess carbohydrates are shuttled to the placenta, providing a source of energy for fetal growth (2). Inefficiency in transporting glucose due to insufficient or ineffective insulin action results in chronic hyperglycemia. Chronic hyperglycemia in pregnancy may result from preexisting pre-diabetes (PD) and type 2 diabetes mellitus (T2DM). Alternatively, previously euglycemic women may develop gestational diabetes mellitus (GDM) due to inability to compensate for the rising insulin resistance (5). Physical activity (PA) has been shown to reduce the risk of adverse outcomes in pregnant women with and without hyperglycemia (6). Despite the abundance of evidence on the benefits of PA in pregnancy (7), several factors (8-12) contribute to the dismal amount of activity among pregnant women (13).

GESTATIONAL DIABETES MELLITUS

Gestational diabetes, or hyperglycemia first recognized during pregnancy, typically resolves at, or shortly after, delivery (14). According to a study based on data from the 2007-2014 National Health and Nutrition Examination Survey (NHANES), the estimated prevalence of GDM in the U.S. is 7.6% (15). However, due to variable diagnostic criteria and screening methods throughout the years from various governing bodies (Table 1), incongruent prevalence estimates for GDM exist (16,17). Screening and diagnostic tests are typically given at 24-28 weeks gestation (18,19). The most common screening method in the U.S. is the 50g, 1-Hour (H) oral glucose tolerance test (OGTT), endorsed by the American Diabetes Association (ADA) and the American College of Obstetricians and Gynecologists (ACOG) (20, 21) (Table 1). Diagnostic methods may be one-step or two-step with the 50g 1-H OGTT included as an initial screen. The one-step diagnostic method endorsed by the The International Association of Diabetes Pregnancy Study Groups (IADPSG) and the ADA are the fasting plasma glucose (PG), and the 1-H and 2-H OGTT following a 75g glucose load (18). Diagnostic criteria for GDM include a fasting PG between 92 and 125 mg/dl, a 1-H PG ≥180 mg/dl and a 2-H PG between 153 and 199 mg/dl following the OGTT (18,19). Additionally, the two-step approach recommended by the ACOG utilizes the initial 50g 1-H OGTT screening prior to the 3-H OGTT following a 100g glucose load (21) (Table 1. Furthermore, diagnostic demarcation points for fasting PG vary depending on the test given.

Women with GDM are at a seven-fold increased risk for developing T2DM (22) and a 50% increased risk for developing cardiovascular disease (CVD) (23). Furthermore, one-third of women with GDM develop postpartum depression (24). Other sequelae include increased risk for perinatal mortality, fetal macrosomia, neonatal hypoglycemia, caesarean section, and

postpartum depression (25). Moreover, their offspring are at a higher risk for glucose intolerance, T2DM, and obesity.

	Screen	Diagnosis
IADPSG (19)	None	2 h 75 g OGTT Diagnosis if 1 or more glucose ≥: Fasting 5.1 mmol/L (92 mg/dL), 1 h 10.0 mmol/L (180 mg/dL), 2 h 8.5 mmol/L (153 mg/dL)
ACOG (21)	50 g glucose challenge test Abnormal: can choose from 7.2 mmol/L (130 mg/dL), 7.4 mmol/L (133 mg/dL), or 7.8 mmol/L (140 mg/dL)	3 h 100 g OGTT Diagnosis if 2 or more ≥: Fasting 5.3 mmol/L (95 mg/dL), 1 h 10.0 mmol/L (180 mg/dL), 2 h 8.6 mmol/L (155 mg/dL), 3 h 7.8 mmol/L (140 mg/dL) or Fasting 5.8 mmol/L (105 mg/dL), 1 h 10.6 mmol/L (190 mg/dL), 2 h 9.2 mmol/L (165 mg/dL), 3 h 8.0 mmol/L (144 mg/dL)
ADA (20)	One-step: none or Two-step: see ACOG	One-step: see IADPSG or Two-step: see ACOG
Diabetes Canada (26)	Preferred approach: 50 g Glucose challenge test Abnormal if \geq 7.8 mmol/L (140 mg/dL) Diagnostic if \geq 11.1 mmol/L (200 mg/dL) Alternative approach: None	Preferred approach: 2 h 75 g OGTT Diagnosis if 1 or more ≥: Fasting 5.3 mmol/L (95 mg/dL), 1 h 10.6 mmol/L (190 mg/dL), 2 h 9.0 mmol/L (162 mg/dL) Alternative approach: See IADPSG
WHO (27)	None	<u>a</u>

Table 1. Screening and diagnostic recommendations for (4)	Table 1. Screenin	g and diagnostic	recommendations	for GDM
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а

As of March 8, 2018, this statement has been added: "WHO currently does not have a recommendation on whether or how to screen for GDM, and screening strategies for GDM are considered a priority area for research, particularly in LMICs."

Note. Adapted from "Chapter 22- Gestational Diabetes and Type 2 Diabetes During Pregnancy" by Mukerji, Bacon & Feig. *Maternal-Fetal and Neonatal Endocrinology*. 2020:371-388. Copyright © 2020 Elsevier Inc. All rights reserved.

PREDIABETES

An estimated 36% of women in the U.S. have PD (14). The screening methods outside of pregnancy are the same as with T2DM: fasting PG, 2-H OGTT with a 75g glucose load, and glycosylated hemoglobin (A1C) (18). Demarcation points for PD diagnosis are fasting PG, 2-H PG, and A1C ranging from 100-125 mg/dl, 140-199 mg/dl, and 5.7-6.45%, respectively. Although PD is not as detrimental as T2DM, 5-10% of patients with PD progress to T2DM annually (28). Though similar recommendations are made for T2DM and GDM, particular emphasis on weight loss of 5-10% of body weight and 30 minutes a day of moderate intensity aerobic activity (AA) is recommended as a first line treatment for patients with PD for prevention of progression of disease severity (28).

TYPE 2 DIABETES MELLITUS

Nearly 14% of the total population of U.S. women have T2DM, with the prevalence increasing with age (14). Approximately 2.9% of women of a reproductive age have been diagnosed with diabetes (29). A 2005-2006 report in Ontario, estimated 4.3/1000 cases of T2DM in pregnancy (30). Risks associated with T2DM are diverse and can have life-altering implications such as augmented risk for CVDs (31). Other serious consequences include blindness, kidney failure, lower limb amputations, cardiovascular events, and complications in pregnancy (1,27). A patient must have two abnormal test results from the same test to confirm T2DM diagnosis. Demarcation points for T2DM diagnosis are as follows: fasting PG \geq 126 mg/dl, 2-H PG \geq 200 mg/dl, and A1C \geq 6.5% (18).

PHYSICAL ACTIVITY IN PREGNANCY

Pregnancy is a unique time in a woman's life where her daily activities impact both herself and her unborn child. Therefore, PA recommendations are made with both maternal and neonatal health in mind. The 2020 ACOG recommend that all pregnant women without complications stay active and engage in both aerobic and strength conditioning exercises (7). In the absence of further evidence of PA dosage, ACOG supports the 2018 guidelines for PA in pregnancy set out by the U.S. Department of Health and Human Services (DHHS) (32). According to the guidelines, pregnant women should engage in at least 150 minutes of moderate intensity aerobic activity (AA) throughout the week (32). Moderate intensity is defined as any activity that is 3-4 METS, or the equivalent to brisk walking (33). Healthy pregnant women who regularly engage in vigorous AA can continue but should communicate with their healthcare provider on how to safely do so as the pregnancy progresses (2). Current U.S. recommendations do not include muscle strengthening activity (MSA) recommendations for pregnant women. However, the 2019 Canadian Guidelines for Physical Activity throughout Pregnancy (3) do generally encourage resistance training.

In addition to PA recommendations for overall wellness, specific recommendations are also made for management of GDM and T2DM in pregnancy (34) In line with the 2018 DHHS guidelines for PA in pregnancy, the Fifth International Workshop-Conference on Gestational Diabetes recommended moderate intensity PA for 30 minutes a day on most days of the week for management of GDM (35). Similarly, the ADA recommends women with pre-existing diabetes of any kind to engage in 20-30 minutes of moderate intensity PA on most days of the week, prior to and during pregnancy (36). The ACOG has previously listed absolute and relative contraindications to exercise in pregnancy (37). However, absolute contraindications are uncommon. Relative contraindications, such as poorly managed type 1 diabetes, may be addressed by consulting with a specialist, appropriate diet, and individualized exercise programming (7). In addition, pregnant women are advised against participating in contact sports, high fall risk sports, scuba diving, sky diving, and exercising in hyperthermal environments such as in hot yoga. Due to lack of evidence, bedrest is no longer recommended in women at risk for preterm birth or preeclampsia (38,39). Bedrest increases the chances of venous thromboembolism, bone demineralization, and deconditioning (38).

Several health benefits may occur in physically active pregnant women. In a randomized control trial of 62 pregnant women, the aerobic PA group (n=31) improved both aerobic fitness and muscular strength, when compared to sedentary controls (P<0.05). Furthermore, there were fewer caesarean sections and faster postpartum recovery in the exercise group (p<0.05) (40). The inverse relationship between PA and caesarean deliveries has been extensively published (41-43). Moreover, PA has been found to be inversely associated with preeclampsia (44). A meta-analysis of 40 observational studies reported a 30% reduction in GDM risk for any general inclusion of PA (45). Physical activity improves blood sugar levels by restoring insulin sensitivity and minimizing glucose intolerance (46Structured exercise programs may reduce the risk of GDM by 30% (47). In a 2017 randomized controlled trial of 300 overweight or obese pregnant women, 30 minutes of cycling three times per week, beginning in the first trimester until 37 weeks gestation, significantly reduced incidence of GDM (22.0% vs 40.6% in the control group; P < 0.001).

Although less researched, some evidence exists for the benefits of MSA in pregnancy. In a clinical trial of 26 pregnant women, low to moderate intensity strength training two days per week for 12 weeks transiently improved mental and physical energy levels and reduced fatigue, independent of AA (48). A study of 139 pregnant women revealed that feelings of energy were increased and fatigue symptoms were reduced among 56 pregnant women who completed 50 minutes of unspecified strengthening and stretching exercises of an unspecified intensity that involved exercise-balls, Pilates, and yoga type movements (49).

ESTIMATED PREVALENCE OF PHYSICAL ACTIVITY IN PREGNANCY

Based on 2010-2015 National Health Interview Survey data, only one-third of adult women meet the recommended 150 minutes moderate intensity AA (or vigorous equivalent) and two days of MSA per week (50). Moreover, a 2007-2014 NHANES study reported only 23% of pregnant women in the U.S. met the recommended 150 minutes of moderate intensity AA and only 12% did so by exercising throughout most of the week (51). Accelerometry data from 2003-2006 NHANES reported roughly one-third of all women did not engage in any PA during pregnancy (52). Thus, clinicians are likely to more often encounter women who are inactive or insufficiently active. Additional factors associated with meeting PA recommendations are education level, age, non-Hispanic white race, being unmarried, not smoking, higher income, and general health status (53).

BARRIERS TO PHYSICAL ACTIVITY IN PREGNANCY

Although the benefits of exercise in pregnancy have been widely published, there are several factors that may negatively impact exercise behavior in pregnant women.

In a systematic review examining correlates of PA in pregnancy, mental health, prior PA, self-efficacy, and intention to be physically active have among the strongest effect sizes contributing to PA engagement (54). A 2017 review of qualitative and quantitative evidence revealed that lack of time due to work, tiredness, pregnancy-related symptoms, and lack of social support were among the most prominent barriers to PA participation. Furthermore, despite the ACOG recommendations on the benefits of exercise, there is a prevailing fear related to risk of miscarriage, growth restriction, pre-term birth, fatigue, and harm to the fetus, among patients and clinicians (55).

Exercise programs led by a trained professional (i.e., exercise physiologist) may mitigate some of these fears and bypass barriers related to lack of knowledge (56) and motivation (55). One study examined the efficacy of at home versus face-to-face exercise programming with a trainer for women with GDM (57). The intervention took place from about 20 weeks to 32 weeks of gestation. At the 32-week follow up, women receiving the face-to-face intervention had a higher number of pedometer steps per day, significantly higher exercise minutes (p<0.05), and positive motivational determinants (attitude, subjective norm, perceived control, intention). Moreover, postprandial blood glucose after 36 weeks of gestation was lower in the face-to face group than the at home group.

ABBREVIATED LITURATURE REVIEW

Normal physiological changes leading to insulin resistance in a healthy pregnancy may be exacerbated in women with overt diabetes and undetected endothelial dysfunction, leading to maternal hyperglycemia (2). Numerous studies demonstrate the role of PA before and during pregnancy in reducing the risk of maternal hyperglycemia (37,58-60). Furthermore, pregnant women who have already been diagnosed with hyperglycemia can improve their glycemic control through PA (46,61,62). Risk factors associated with maternal hyperglycemia such as older age (25), minority ethnicity, elevated BMI, having children, and education level, have also been tied to PA participation (23). Exercise interventions have explored various methods of reaching this population to promote PA by tackling social, cognitive, and emotional barriers (63-66).

PURPOSE AND STUDY AIM

To our knowledge, this is the first study to examine PA in GDM and PD together as one high-risk for diabetes group. This study adds to the evidence demonstrating differences in PA engagement among pregnant women at high-risk for diabetes, overt diabetes, and no diabetes. Therefore, we aim to answer three questions:

1. Is there an association between diabetes risk status (DRS) and meeting the 2008 DHHS recommendation for PA in pregnancy?

2. Is there an association between DRS and engaging in the DHHS adult recommendation of at least two days of MSA per week in pregnant women?

3. What are the major characteristics that are associated with meeting the pregnancy PA recommendations and two days of MSA?

PROJECT DESCRIPTION

This secondary analysis used data from the Behavioral Risk Factor Surveillance System (BRFSS) in the interview years, 2011, 2013, 2015, and 2017. Only the odds years between 2011 and 2017 were used due to more in-depth PA questions. The population sample was limited to pregnant women between the ages of 18-44 who had complete data on all the variables of interest. Further exclusion of probable type 1 diabetes brought the population sample size to 9,597 participants. Women with self-reported GDM and PD were identified as the high-risk for diabetes (HRD) group. Women with self-reported diabetes were in the diabetes mellitus (DM) group. Women who reported no diabetes were in the no-diabetes (ND) group. Aerobic activity and MSA were dichotomized into 'meets,' and 'does not meet,' the 2008 DHHS PA guidelines.

Note that the 2008 DHHS recommendations are used as the standard of measurement instead of the more recent 2018 DHHS recommendations. This is due to the survey designs of the 2011, 2013, 2015, and 2017 BRFSS, where duration of a single bout of reported PA that is under 10 minutes is not counted. New guidelines allow for a minimum of 2-minute bouts. Therefore, an accurate measurement of meeting the 2018 guidelines cannot be ascertained from the present data. Furthermore, all data utilized in this project was collected prior to the release of the 2018 PA guidelines.

Other limitations to the study are as follows:

- 1. Due to the cross-sectional study design, we cannot infer causality.
- 2. All data was self-reported; therefore, all data is subject to recall bias.

- 3. There are no objective measures.
- 4. Contraindications to exercise may exist but we are unable to obtain this information from the survey.
- 5. We cannot control for adiposity due to lack of information on pre-pregnancy BMI.

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Chapter Two: Review of Literature

The chronic hyperglycemia seen in gestational diabetes mellitus (GDM), prediabetes (PD, and type 2 diabetes mellitus (T2DM) is a result of insulin resistance (1) and can lead to adverse health outcomes during and after pregnancy (2-8). In 2017, the estimated worldwide prevalence of combined GDM and pre-existing diabetes in pregnancy was 16.2% (9). Symptoms of hyperglycemia include polyuria, polydipsia, polyphagia, and increased sensitivity to certain infections (10).

Pregnancy is an opportunity in a woman's life for establishment of healthy lifestyle practices that carry maternal and fetal benefits (11). The American College of Obstetricians and Gynecologists (ACOG) recommend physical activity (PA), as it is linked to prevention of GDM, other cardiometabolic diseases and pregnancy complications (11,12). The factors leading to PA engagement are complex and may be related to factors contributing to diabetes.

This chapter includes a discussion of the hormonal and immunological changes in pregnancy leading to insulin resistance, a history of hyperglycemia in pregnancy, definitions and diagnoses of T2DM, GDM, and PD, an overview of adverse outcomes due to hyperglycemia, risk factors associated with diabetes, evidence of PA for improved glycemic control and GDM prevention in pregnancy, potential barriers to engaging in PA, and exercise interventions.

BIOLOGICAL MECHANISMS OF HEALTHY AND HYPERGLYCEMIC PREGNANCIES

During the second half of pregnancy, skeletal muscle attenuates the glucose disposing actions of insulin by about 50% to accommodate the energy needs of the fetus (13). Insulin resistance arises from a combination of hormonal changes and is part of the natural physiology associated with a healthy pregnancy. The pathological outcomes of hyperglycemia in pregnancy arise from the coexisting issues related to insulin resistance and endothelial dysfunction (14-17). This section will cover key issues in the progression of physiological insulin resistance and identify distinguishing characteristics of pathological insulin resistance in pregnancy.

Reduced insulin signaling during pregnancy is partially due to attenuated adiponectin action. Adiponectin, a protein made in adipocytes, placenta, and skeletal muscle (18,19), acts as an insulin sensitizer by activation of peroxisome proliferator-activated receptor and 5' adenosine monophosphate-activated protein kinase in both the skeletal muscle and liver, inducing glucose transporter type-4 (GLUT4) translocation and fatty acid β -oxidation (20). Adiponectin levels normally decline slightly in late pregnancy (21).

Leptin, also made by adipose tissue (22), placenta (23), and skeletal muscle (24), possess insulin sensitizing actions (22). Secretions of leptin peak during the late 2nd and early 3rd trimester, leading to greater fat accumulation, satiety, and fatty acid oxidation in skeletal muscle (25). Leptin increases glucose uptake by stimulation of sympathetic nerves and B2 adrenergic receptors in myocytes (26). Over the course of pregnancy, the downregulation of the OB-Rb receptor induces leptin resistance, decreasing energy intake into cells of the mother (27).

The increase in sex hormones (28), progesterone (Pg) and estrogen may also play a role in the desensitization of insulin receptors. Higher concentrations of Pg may reduce expression of insulin receptor substrate (IRS)-1 and inhibit insulin-induced GLUT4 translocation and glucose uptake into skeletal muscle (29). Animal studies on pregnant rats have demonstrated that estradiol (E2) does the opposite- increasing receptor binding as well as expression and membrane translocation of GLUT4 in adipocytes (30). During late pregnancy, higher levels of E2 repress GLUT4 expression in skeletal muscle (31) and a reduction in insulin binding is induced by Pg, cortisol, prolactin, and human placental lactogen (hPL) (32).

The prolactin family, hPL and human placental growth hormone (hPGH) are produced in early pregnancy and gradually increase during gestation, contributing to the progression of insulin desensitization in skeletal muscle (13,33). Early in pregnancy, hPL stimulates the growth of pancreatic islets, increasing insulin secretion (34). In mid to late pregnancy, hPL stimulates 3H-thymidine incorporation, insulin gene transcription and production, and glucose-dependent insulin secretion in pancreatic islet cells which may lead to postprandial hyperglycemia and hyperinsulinemia (35). Insulin resistance could also be induced by hPL binding to the growth hormone receptor (32). Insulin signaling may be further limited by hPGH action (13).

Tumor necrosis factor- alpha (TNF- α), a cytokine produced by white blood cells, fibroblasts, adipocytes, and the placenta, may impair insulin signaling by acting as a serine/threonine kinase of insulin receptor substrate (IRS) – 1 (35). Additionally, in mid to late pregnancy, TNF- α suppresses the transcription of adiponectin (13).

Abnormal hormone responses in pregnancy present in women with GDM and T2DM (14,15,17,36). Women with T2DM exhibit impaired vascular reactivity and an attenuated response to estrogen stimulation (14,15,36); whereas, estrogen contributes to enhanced insulin

resistance in women with GDM (17). Additionally, lower levels of adiponectin in pregnancy correlate to diagnosis of GDM (37).

The differentiation between insulin resistance in normal and hyperglycemic pregnancies is due to divergence in specific mechanisms leading to glucose transport. A BMI and agematched study compared glucose transport activity and expression and phosphorylation of the insulin receptor and IRS-1 in women with GDM (n=7), pregnant women without GDM (n=11) and non-pregnant women (n=11) (38). Biopsies from the rectus abdominus were obtained from the three groups. Findings revealed a 32% lower rate of maximal insulin-stimulated 2deoxyglucose transport in the non-GDM pregnant group when compared to the non-pregnant control. Moreover, there was an additional 54% lower rate in the GDM group when compared to the non-GDM pregnant group (P<0.05). The maximal effect of insulin on tyrosine phosphorylation of the insulin receptor was 37% lower in the GDM group versus the non-GDM pregnant group (P < 0.05). There was a 23% (P < 0.05) and 44% (P = 0.002) reduction in the IRS-1 protein levels in muscle from non-GDM and GDM pregnant women, respectively. Although based on a small number of women, the findings of this study indicate that insulin resistance to glucose transport during pregnancy is associated with a decrease in IRS-1 tyrosine phosphorylation, mainly due to decreased expression of IRS-1 protein. In pregnant women with GDM, a decrease in tyrosine phosphorylation of the insulin receptor beta-subunit is associated with further decreases in glucose transport activity (38).

Higher concentrations of inflammatory biomarkers have also been associated with hyperglycemic conditions. Garcia et al. (39) discusses the relationship between diabetes and inflammation. Inflammation may coexist or amplify diabetes by toll-like receptor pathways that detect liposaccharides (LPS). Saturated fatty acids stimulate production of TNF-α and interleukin (IL-6). Obesity-induced diabetes propagates in part by high LPS levels that stimulate certain inflammatory response proteins in endothelial cells, which is also associated with insulin resistance. High stress levels (i.e., from poor lifestyle choices) can increase blood pressure through the sympathetic nervous system, thereby promoting inflammatory effects on the endothelium. This can promote interleukin synthesis, which is a potential biomarker of diabetes and PD. Abnormally high neutrophil-platelet volumes exist in those with PD and diabetes and, therefore, reliably marks the presence of inflammatory marker, is seen in higher serum concentrations in women with GDM. IL-6 and C - reactive protein (CRP) are both verifiable inflammatory biomarkers of diabetes in women. TNF- α , IL-6, CRP, vascular adhesion molecule- 1, intercellular adhesion molecule, E- and P-selectins, von Willebrand Factor, plasminogen activator inhibitor 1, fibrinogen and adiponectin, may also be associated with the development of T2DM (39).

In summary, insulin resistance in pregnancy arises from myriad biochemical mediators. Increased insulin resistance may be exacerbated by underlying, endothelial dysfunction. This increase in insulin resistance leads to compromised glucose transport, leading to hyperglycemia.

HISTORY, DEFINITIONS, AND DIAGNOSIS OF HYPERGLYCEMIA IN PREGNANCY

The conglomeration of increased GDM (40), PD, and T2DM (41) in women of a childbearing age has led to the rising prevalence of hyperglycemia requiring clinical management in pregnancy (9). In 2013, a global estimate of 21.4 million women had

hyperglycemia in pregnancy (42). Environmental factors and universal screening for all asymptomatic pregnant women are largely responsible for this uptrend (43, 44)

Classification of hyperglycemia has evolved. In 2010, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) created three categories for hyperglycemia in pregnancy: pre-gestational diabetes (PGDM), overt diabetes first recognized in pregnancy (DIP), and GDM (45). Three years later, the World Health Organization (WHO) followed suite, implementing this categorization as well (46). Pre-gestational diabetes is defined as established diagnosis of hyperglycemia prior to pregnancy. Gestational Diabetes Mellitus (GDM) is unregulated blood glucose that initiates during pregnancy and terminates after delivery (47).

Prior to the First International Workshop on GDM in 1980, the American Diabetes Association (ADA) recommended glucose screening in pregnant women at a higher risk for diabetes. As universal screening became more widely adopted, prevalence rates of GDM grew. Hyperglycemia and Adverse Pregnancy Outcomes Study (HAPO), published in 2008, reinforced the negative implications of hyperglycemia below levels of overt diabetes in pregnancy. Specifically, they highlighted the strong, continuous association of maternal glucose levels with increased birth weight and increased cord-blood serum C-peptide levels.

Prediabetes, also called borderline diabetes, in pregnancy has not been well researched, in part because PD often goes undiagnosed until pregnancy, when it is then classified as GDM (48). The oral glucose tolerance test (OGTT) is the most widely accepted method of assessing hyperglycemia in pregnant women without PGDM. According to the 2013 WHO Recommendations, a diagnosis of GDM is valid if the fasting plasma glucose (FPG) is 5.1-6.9 millimoles per liter (mmol/L) (92-125 mg/dl, the 1-hour (h) PG is \geq 10.0 mmol/L (180 mg/dl) following a 75 g oral glucose load, or the 2-h PG is 8.5-11.0 mmol/L (153 -199 mg/dl) following a 75g oral glucose load. Plasma glucose values above the upper demarcation points are grounds for diagnosing DIP (46).

Diagnostic criteria for women with PD and T2DM include the fasting PG and OGTT along with a glycohemoglobin (A1C) test. The A1C test is not recommended for diagnosing diabetes in pregnancy due to equivocal findings and increases in red blood cell turnover in pregnancy (49). Pre-gestational diabetes is confirmed by a FPG of \geq 126 mg/dl, an OGTT two-h PG \geq 200 mg/dl after a 75g oral glucose load, or a A1C concentration of \geq 6.5%. Diagnosis for PD in non-pregnant women is a fasting PG between 100 and 125 mg/dl, an OGTT 2-h reading between 140 and 199 mg/dl or an A1C from 5.7 to 6.4% (50).

RISK FACTORS

There are several factors associated with maternal hyperglycemia; being above the age of 25, an abnormal body weight before pregnancy, being a member of an ethnic group (e.g., Filipino and Hispanic) with a high prevalence of GDM, immediate family members with a history of diabetes, a history of abnormal glucose tolerance, or a history of poor obstetric outcome (4). African American and Hispanic women are particularly susceptible to diabetes compared to other racial minorities (51). Education level has been shown to be a predictor of T2DM and potential predictor of GDM (52). Alcohol consumption in moderation has been shown to reduce the likelihood of diabetes (53). However, excessive consumption may have deleterious effects on glycemic control. Smoking status is also associated with poor glycemic control (54). A consistent, positive dose response exists between BMI and outcomes of GDM

(55). Overweight women are twice as likely, obese four times more likely, and severely obese eight times more likely to acquire GDM.

Endothelial dysfunction, a hallmark of PD, is strongly associated with T2DM (56). The metabolic pathways leading to T2DM are closely associated with cardiovascular diseases, hypertension, and lipoprotein metabolism. Type 2 diabetes bears a robust association with environmental risk factors and accounts for 90-95% of those with diabetes. This type of diabetes relates closer to obesity/adiposity more than with type 1 diabetes (50).

ADVERSE OUTCOMES

Gestational diabetes mellitus patients face more than a seven-fold increased risk in developing T2DM (3,57). The first five years after delivery has been identified as a critical window in which this risk is greatest (58). Indeed, even without GDM, five to ten percent of patients with PD progress to T2DM annually (7).

Potential permanent consequences to diabetes includes loss of vision, renal failure, and peripheral neuropathy, amputations, Charcot joints (neuropathic joint), and foot ulcers (50). The estimated economic burden of diabetes in 2017 was \$327 billion (59). The average female with diabetes incurs about \$9110 per year in medical costs for diabetes alone (59). The projected increase in diabetes prevalence in the US before 2030 is 1.0 million per year (60). By this estimate, by 2060 19.6% of all women in the US will have diabetes compared with the 9% prevalence in 2014 (a potential 118% increase). The interconnection of insulin resistance, endothelial dysfunction and atherosclerosis reinforces the relationship between T2DM and vascular diseases such as coronary artery disease (56).

After the first diagnosis of GDM, the risk of developing another metabolic condition escalates (61). When a nulliparous woman receives the diagnosis, she has a 41% higher risk of developing GDM again during a subsequent pregnancy. A study compared glucose tolerance, insulin levels, biochemical parameters, and brachial vasodilatory responses between 16 obese, 17 non-obese women previously diagnosed with GDM, and 19 healthy non-obese women (62). Results revealed a reduced flow-mediated dilation in the brachial arteries of women with normal glucose tolerance but a history of GDM, signifying vascular impairment. Non-obese women with a history of GDM also had high uric acid levels, a marker of insulin resistance, suggesting an association between hyperglycemia in pregnancy and post gravid metabolic dysfunction independent of adiposity.

The HAPO study brought to light pregnancy-related sequelae that arise from hyperglycemia below established PD and GDM levels (63). Such negative implications included preeclampsia, hyperbilirubinemia, intensive neonatal care, shoulder dystocia/birth injury, premature delivery before 37 weeks, high cord-blood serum C peptide, clinical neonatal hypoglycemia, primary cesarean section, and birth weight >90th percentile. A prospective study in south India found that mothers with GDM have a mean body weight of 9.9 kg more than controls (2). Their BMI was 28.8 vs 25 in the control group. Neonatal complications associated with the GDM pregnancies included macrosomia, premature pregnancy, sacral agenesis, ventricular septum tumor syndrome, hypoglycemia, respiratory distress, and death (2). Obesity further complicates women with maternal hyperglycemia, heightening their chances of developing preeclampsia and metabolic syndrome. Women with maternal hyperglycemia and higher BMIs also give birth to more babies with macrosomia, hypoglycemia, and fetal diabetes (6). In addition to these consequences, T2DM in pregnancy can amplify the severity of these outcomes and contributes to higher likelihood of congenital abnormalities and stillbirth (64).

Children exposed to hyperglycemia in utero face additional dangers. These children are at a higher risk for coronary artery disease and atherosclerosis (65,66) as well as glucose intolerance, T2DM, and obesity (4). According to a cross-sectional study using the California Cancer Registry from 1988 to 2013, several childhood cancers such as acute lymphoblastic leukemia and Wilm's tumor were associated with pre-pregnancy diabetes as well as maternal overweight conditions (66).

PHYSICAL ACTIVITY RECOMMENDATIONS, BENEFITS, BARRIERS, AND INTERVENTIONS

RECOMMENDATIONS

Table 1 summarizes considerations relevant to pregnancy for implementing an exercise prescription. Specific recommendations such as moderate intensity and thermoneutral environment are made to prevent fetal stressors (12).

Specific clinical recommendations have been made for women with hyperglycemia (67). Preconception counseling and lifestyle changes are recommended in women with pre-existing T2DM and GDM, respectively. Both recommendations include PA promotion during pregnancy. First line treatment in PD for prevention of overt diabetes includes weight loss of 5-10% of body weight and 30 minutes a day of moderate intensity physical activity (PA) (7).

	First Trimester, More than 12 Weeks of gestation
Duration of session	30-60 minutes
Times per week	At least 3-4 (up to daily)
Intensity of exercise	Less than 60-80% of age-predicted maximum maternal heart rate*
Environment	Thermoneutral or controlled conditions (air conditioning; avoiding prolonged exposure to heat)
Self-reported intensity of exercise (Borg scale ^a)	Moderate intensity (12-14 on Borg scale)
Supervision of exercise	Preferred, if available
When to end	Until delivery (as tolerated)

 Table 1. Characteristics of a Safe and Effective Exercise Regimen in Pregnancy

*Usually not exceeding 140 beats per minute; ^a Borg scale is a 15-category scale (from 6-20) to measure the level of perceived exertion: light exercise is approximately 6-11; 13 is somewhat hard; 15 is hard; 19 is extremely hard

Note: Adapted from "Exercise is pregnancy! " by Berghella V, Saccone G. *Am J Obset Gynecol*. 216:335-7, 2017. Copyright

BENEFITS OF EXERCISE AND PHYSICAL ACTIVITY

Exercise plays a crucial role in prevention and treatment of hyperglycemia in pregnancy through counteraction of metabolic pathways associated with increased glucose uptake, hypertension, chronic systemic inflammation, dyslipidemia, and oxidative stress (68).

A multitude of observational studies have examined the positive impact PA plays in treatment and prevention of hyperglycemia in pregnancy. A meta-analysis of 40 observational studies reported a 30% reduction in GDM risk for any general inclusion of PA (69). A prospective cohort study assessed pre and current pregnancy PA and incidence of GDM in 909 women in Tacoma, Washington (70). When compared to inactive women, they observed a 56% risk reduction in GDM incidence (RR 0.44; 95% CI 0.21-0.91) for any participation of PA in the year before pregnancy. Additionally, a 76% risk reduction in GDM incidence (RR 0.24; 95% CI 0.10-0.64) was observed for women engaging in at least 4.2 hours/wk of pregravid PA. Physical activity both before and during pregnancy resulted in a 69% reduction in the GDM incidence risk (RR 0.31; 95%CI 0.12, 0.79) when compared to inactive women. Previously inactive women who decide to participate in PA during pregnancy can reduce their chances of developing GDM. In a study using data from the 1988 National Maternal and Infant Health Survey (71), 4,813 women who reported being physically inactive before pregnancy, with singleton births and no previous diabetes diagnosis were examined. Findings revealed 57% lower adjusted odds (OR 0.43, 95% CI 0.20-0.93) of developing GDM in women who became physically active when compared to those who remained inactive in pregnancy.

Various randomized controlled trials (RCTs) with different modes of exercise have also shown improvements in glycemic measures. One RCT including 342 pregnant women from Spain examined the effectiveness of exercise beginning in early pregnancy (~12 weeks) on GDM incidence. The intervention group (n=101) exercised for 60 minutes on land and 50 minutes in water 3x/wk. At the end of the trial, there was a lower prevalence of GDM in the exercise group (n=1) than in the usual care group (n=8) (P=0.009) (72). Another RCT aimed to find the effect of exercise on PG levels in 41 parous women (20-33 weeks' gestation) with persistent fasting hyperglycemia between 105 and 140 mg/dl (73). Subjects were either treated with insulin (control) or exercised on a cycle ergometer at moderate intensity 3x/wk. As a result of the exercise intervention, pregnant women had regulated blood glucose levels in normal range for the rest of their pregnancy and did not require insulin . Furthermore, one study took (n=19) women with gestational diabetes to perform upper arm ergometry 3x/wk, 20 min each session, 50% VO2max (74). Findings demonstrated a normalization in glycemic control after 4 weeks, as opposed to diet alone.

Leisure-time physical activities (LTPA) have been shown to lower the chances of developing diabetes and PD (75,76). One prospective study of 21,630 men and women in Finland assessed the relationship of occupational, commuting, and LTPA with the incidence of T2DM (75). Measurement of the three types of PA were ascertained through surveys administered in 1982, 1987, and 1992. The National Hospital Discharge Register and the National Social Insurance Institution's Register were linked to the study participants to identify T2DM incidents. Notably, women who had high occupational PA levels had the highest mean BMI, systolic blood pressure, and obesity prevalence. There was no significant association between occupational PA and T2DM in women. Commuting PA exhibited a significant inverse relationship with T2DM in women.

Strength training in women with hyperglycemia may prove especially beneficial because glucose disposal occurs primarily in the skeletal muscle cells (13). Morais, et al. compared cardiovascular and strength interventions in older adults with and without diabetes by measuring the circulating microRNA (c-miR) concentrations of c-miR-126, c-miR-146a, and c-miR-155, which are associated with lower PG levels (77). Results indicate an increase in c-miR in PG and particularly c-miR-146a levels in those who engage in strength training. Both T2DM and control groups increased plasma levels of c-miR with a greater increase in the T2DM group. The increase c-miR-146a plasma levels have a reported negative association with blood glucose levels. Interestingly, those in a subgroup performing only cardiovascular interventional training did not have any change in c-miR-146a regardless of diabetes status . This and other studies illuminate the role of resistance training on the prevention of T2DM and its effect on

inflammation. A 2015 study utilizing data from the 1999-2004 National Health and Nutrition Examination Survey found that women who engaged in muscle strengthening activity (MSA) had significantly lower levels of CRP (78).

BARRIERS

Despite clinical recommendations, evidence suggests low adherence to adequate PA requirements in pregnant women and non-pregnant women with a history of GDM (hGDM) and current diabetes. One study using 2001-2003 BRFSS data reported that women with hGDM are not more likely to adopt healthy lifestyle behaviors than their non-GDM counterparts, suggesting that awareness of disease does not positively influence change in behavior (79). Another study using 2003 BRFSS data observed approximately 57.4% of the hGDM group and 70.9% of the current diabetes group did not meet the PA recommendations. Moreover, women reporting to currently have diabetes or hGDM were significantly more likely to engage in no LTPA (OR 1.4 and 1.4 respectively; P<0.05) and to fail to meet the national PA recommendations (OR 1.4 and 1.2 respectively; P<0.05) (80). Smith et al. studied the prevalence of meeting PA guidelines using METs to assign sufficient PA, low PA, or sedentary behavior (81). A survey was given to 226 women who had previously been diagnosed with GDM. Of the 226 women, 26.1% were sedentary, 39.4% had low PA levels, and 33.2% were sufficiently active. Most of the women with enough activity were English speaking. An estimated 48.9% of participants reported not knowing what PA level would be enough for prevention of diabetes. Swan et al. indicated that 58% of women were in a pre-action stage for strenuous activity and, therefore, inactive (82,83). After a comprehensive review of eighteen studies, Kaiser

and Razurel concluded that compliance to the PA recommendations was inadequate in this population (84).

A unique combination of factors contributes to exercise decisions in pregnancy. Among them are lack of knowledge on sport and exercise, inconvenience (85), other health problems, low self-efficacy (86,87), lack of time due to work and childrearing (88), tiredness, pregnancyrelated symptoms, lack of social support, and uncertainty on the risk of adverse pregnancy outcomes (89). In an analysis of determinants of health behaviors among women with GDM (90), the "attitudes towards weight loss" scale was independent of PA participation. Emotional encouragement and self-efficacy were significant in determining PA levels.

Socioeconomic status (SES) has been shown to be associated with PA engagement. In a cross-sectional cohort (n=986) study using data from the Midlife in the United States (MIDUS) 1, MIDUS 2, and MIDAS 2 biomarker trials, SES and PA were examined and compared with gluco-regulation (76). Socioeconomic status disadvantage scores and PA levels were obtained using survey responses. Fasting PG and A1C were used to determine glycemic control. After adjusting for confounders, men and women that had childhood disadvantage and adult socioeconomic disadvantage were at lower odds of meeting the PA guidelines in LTPA (OR0.75; 95% CI 0.65–0.86 and OR 0.71; 95% CI 0.62–0.82 , respectively). This study also found an inverse association between engaging in LTPA and odds of developing either PD or diabetes.

Environmental barriers to engaging in PA include social support (91), having children, having a spouse, and space to engage in PA (79). A cross-sectional study of 50,884 women ages 35-74, examined the associations of greenness of residence on PA and obesity (92). Green and natural land cover was assessed using the U.S. National Land Cover Database. Those in the upper tertile of greenness were 17% more likely to expend more than 67.1 metabolic equivalent (MET) h/wk than those in the lowest tertile (OR 1.17, 95% CI 1.10–1.23). Furthermore, the prevalence of obesity was lower for those living closer to green spaces.

PHYSICAL ACTIVITY INTERVENTIONS

Several strategies to increase PA for prevention of adverse diabetes outcomes have been tested. One such strategy involves implementation of the health belief model (HBM), given successful intervention in breastfeeding (a key factor in losing gestational weight gain) in women with GDM (93). However, few programs have proved successful due to the challenges that many of these women face with time, energy, and financial constraints. One diabetes prevention intervention for women with previous GDM in the past three years involved a webbased walking program that utilized pedometers to measure PA level (94). The intervention was based around components of the HBM: risk perception, PA and weight self-efficacy, benefits and barriers to lifestyle change, and "self-regulatory strategies". However, this strategy proved to have no statistically significant (P>0.05) changes in PA outcomes. McIntyre et al. sought to test a social cognitive theory-based program in implementing strategies to encourage PA (95). Results showed some improvement in PA, but minimal. Difficulty in assessing the effectiveness of the program could be due to the small sample size (n=28). Alternatively, a oneyear pilot study measured the effectiveness of a lifestyle intervention based on selfsufficiency and self-motivation (96). The study was rooted in a behavioral, patient centered intervention. Although PA did increase by the end of the year, it was not significant (P>0.05) and several barriers existed in achieving PA goals such as further pregnancies, work and family obligations, childcare, cultural customs, psychosocial stress, and low SES.

A successful four-year lifestyle intervention trial addressed nutrition, breastfeeding, and PA in 586 women (ages 20-49) with prior GDM in Tianjin China (97). Women engaged in at least 30 minutes of moderate or vigorous exercise every day of the week. The Transtheoretical Model was used to gradually taper and maintain goals and encourage self-sufficiency. After one year, mean body weight decreased by 1.4kg. Those who started the trial overweight lost an average of 2.91 kg. Body mass index, waist circumference, percent body fat, serum insulin level, and the homeostasis model assessment- insulin resistance decreased significantly more among women in the intervention group than those in the control group (all P < 0.05).

Social support plays a substantial role in whether enough weekly PA is met (98). Notably, an intervention using Centering Pregnancy groups focused on group meetings, peer support, and learned skills needed for treatment (91). This program had better outcomes in patient PA compliance and neonatal health outcomes than the traditional pregnancy group. Additionally, fewer women in the program required drug therapy or labor induction and there was a significant increase in breastfeeding in the program vs traditional.

SUMMARY

Firmly established is the evidence on the glucose regulating benefits of PA in pregnancy. Physical activity participation has shown to be low in pregnant women and non-pregnant women with a history of GDM and current diabetes. However, associations of GDM, PD, and T2DM in pregnancy and PA participation is not fully understood. Furthermore, risk factors associated with hyperglycemia in pregnancy may also contribute to PA participation. Such factors include racial minority, having children, and lower SES, among others. This review explored the risks and adverse outcomes associated with PD, GDM, and T2DM in pregnant women, PA recommendations for these groups, improved outcomes and potential barriers to PA, and interventions. Interventions implemented a wide range of strategies and exercise modes, addressing various barriers to exercise and PA in women of different ethnicities. Successful interventions included social and emotional support. Furthermore, there is a paucity of research on MSA in pregnancy. Most exercise and PA interventions were centered around AA, with little mention of MSA. Differences in engaging in resistance exercise in pregnant women with varying glycemic conditions is unclear. It is important to identify differences in AA and MSA patterns among pregnant women of varying levels of hyperglycemia in conjunction with potential mediating factors to design effective interventions.

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Chapter 3: Methodology

DATA COLLECTION

This study utilized data from the BRFSS years 2011, 2013, 2015, and 2017. The odd years between 2011 and 2017 were specifically used because of the inclusion of more detailed and comprehensive PA questions. The BRFSS is a survey administered via landlines and cell phones to households in all 50 U.S. states, three U.S. territories, and the District of Columbia (1). The BRFSS obtains information on participant health behavior, healthcare availability, health issues, and demographics. Participants must be 18 years or older to complete the survey. Telephone numbers are randomly sampled in each state or territory by using stratified sampling techniques. Each state may be considered as one stratum, with division into more strata for specific sub-regions. Sub-regions may be disproportionately sampled to provide adequate sample sixes for smaller geographically defined populations. Interviewers are trained specifically for BRFSS and evaluated each year. Calls were made each month of the year, seven days a week, and in the daytime and evening (2).

SAMPLE WEIGHTING

Data weighting is used to ensure that the sample is representative of the adult population in each state. First, the design weight accounts for the probability of selection, nonresponse bias, and noncoverage areas. The weight of each stratum, the number of phones in a household, and number of adults in the household are calculated into the design weight. Second, iterative proportional fitting, or raking, is applied. This weighting adjusts for the demographic differences between those who are interviewed and the represented population. Raking adjusts for one or a combination of demographic categories at a time, in an iterative process. The final weight variable, accounting for design and raking was labeled "_llcpwt"(2). After concatenating survey
years 2011, 2013, 2015, and 2017, a final weight, labeled "finwt", was created in SAS version 9.4. This was done to account for the four years of data collection used and was made by dividing " llcpwt" by four.

SUBJECTS

The total number of pregnant women between the ages of 18-44 in this BRFSS sample was 11,079. Age 44 was used as the age cut-off because the pregnancy question was only asked to women under the age of 45. Women were then excluded if they had incomplete data on variables of interest or if they were first told by a doctor that they had diabetes at age 5 or younger (n=1,482). The latter exclusion was to rule out probable type 1 diabetes mellitus (T1DM). Type 2 diabetes previously accounted for less than 3% of all childhood diabetes cases (3). However, the incidence of T2DM in children has become more common with rising childhood obesity (4). A sensitivity analysis was performed to identify what age would be the best cut-off for the purposes of this study. There was found to be no statistically significant difference (P>0.05) in outcomes based on excluding at any age point, so the conservative threshold of age 5 was used, thereby preserving sample power. After removing all observations with missing information and probable type 1 diabetes, the final sample consisted of 9,597 pregnant women.

CALCULATED VARIABLES

Calculated variables are created by the Centers for Disease Control and Prevention and readily available for use in the data sets. These variables are derived from variables in the data set

by combining, reordering, and applying mathematical procedures. Most of these variables are identified by a leading underscore in the variable name.

PRIMARY DEPENDENT VARIABLES

The primary outcomes of this analysis were calculated from self-reported AA and MSA. Units of measurement for AA and MSA were minutes per week and days per week, respectively.

AEROBIC ACTIVITY

Minutes of AA were examined continuously and were also dichotomized into "meets the AA recommendations" and "does not meet the recommendations". The study sample provided responses to the following questions regarding AA:

13.1 During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?

13.2 What type of physical activity or exercise did you spend the most time doing during the past month? (Participants selected activity/exercise from a list. See Table 1. List of Common Leisure Activities)

13.3 How many times per week or per month did you take part in this activity during the past month?

13.4 And when you took part in this activity, for how many minutes or hours did you usually keep at it?

13.5 What other type of physical activity gave you the next most exercise during the past month?(Participants provided type, frequency, and duration of second activity by responding in the same way as the first activity.)

01 Active Gaming Devices (Wii Fit, 40 Rowing machine exercises Dance, Dance revolution) 41 Rugby 02 Aerobics video or class 42 Scuba diving 43 Skateboarding 03 Backpacking 04 Badminton 44 Skating – ice or roller 05 Basketball 45 Sledding, tobogganing 06 Bicycling machine exercise 46 Snorkeling 07 Bicycling 08 Boating (Canoeing, 47 Snow blowing rowing, kayaking, sailing for pleasure or 48 Snow shoveling by hand camping) 49 Snow skiing 09 Bowling 50 Snowshoeing 10 Boxing 51 Soccer 52 Softball/Baseball 11 Calisthenics 12 Canoeing/rowing in competition 53 Squash 54 Stair climbing/Stair master 13 Carpentry 14 Dancing-ballet, ballroom, Latin, hip 55 Stream fishing in waders hop, Zumba, etc. 56 Surfing 15 Elliptical/EFX machine exercise 57 Swimming 16 Fishing from river bank or boat 58 Swimming in laps 59 Table tennis 17 Frisbee 18 Gardening (spading, weeding, digging, 60 Tai Chi filling) 61 Tennis 19 Golf (with motorized cart) 62 Touch football 20 Golf (without motorized cart) 63 Volleyball 64 Walking 21 Handball 22 Hiking – cross-country 66 Waterskiing 23 Hockey 67 Weight lifting 24 Horseback riding 68 Wrestling 25 Hunting large game – deer, elk 69 Yoga 26 Hunting small game - quail 71 Childcare 72 Farm/Ranch Work (caring for 27 Inline Skating livestock, stacking hay, etc.) 28 Jogging 73 Household Activities 29 Lacrosse 30 Mountain climbing (vacuuming, dusting, home repair, 31 Mowing lawn etc.) 32 Paddleball 74 Karate/Martial Arts 33 Painting/papering house 75 Upper Body Cycle (wheelchair 34 Pilates sports, ergometer 35 Racquetball 76 Yard work (cutting/gathering 36 Raking lawn/trimming hedges wood, trimming, etc.) 37 Running 98 Other 38 Rock climbing 39 Rope skipping

Table 1. List of Common Leisure Activities

Numbers to the left of each activity are identifying codes for estimating MET values.

Activities were assigned estimated metabolic equivalent (MET) values and minutes of moderate or vigorous AA per week were calculated. Finally, the dichotomous variable for meeting the AA recommendations was created.

MUSCLE STRENGTHENING ACTIVITY

Days per week of MSA were calculated by using the responses to the following question: 13.8 During the past month, how many times per week or per month did you do physical activities or exercises to STRENGTHEN your muscles? Do NOT count aerobic activities like walking, running, or bicycling. Count activities using your own body weight like yoga, sit-ups or push-ups and those using weight machines, free weights, or elastic bands.

The dichotomous variable for meeting the MSA recommendations for adults, of at least two days per week, was created.

BOTH AEROBIC ACTIVITY AND MUSCLE STRENGTHENING ACTIVITY

The dichotomous variable for meeting the AA recommendation and engaging in at least two days per week of MSA was created using responses to both AA and MSA questions.

NEITHER AEROBIC ACTIVITY NOR MUSCLE STRENGTHENING ACTIVITY

The dichotomous variable for meeting neither AA or MSA recommendation was created using responses to both AA and MSA questions.

PRIMARY INDEPENDENT VARIABLE

The primary independent variable in this study was derived from self-reported diabetes history. Participants answered the following question: *Has a doctor, nurse, or other health professional EVER told you that you had any of the following? For each, tell me "Yes," "No," or you're "Not sure."*...

6.12 (Ever told) you have diabetes? (117) If "Yes" and respondent is female, ask: "Was this only when you were pregnant?"; If respondent says pre-diabetes or borderline diabetes, use response code 4. The DRS variable was created with three categories: overt diabetes (DM), high-risk for diabetes (HRD), and no diabetes (ND). Women in the DM group answered "Yes" to question 6.12. Women who answered "Yes, but female told only during pregnancy" or "No, prediabetes or borderline diabetes" were in the HRD group. Women who answered "No" were in the ND group.

COVARIATES/DETERMINANTS

The following variables are implemented into the analysis as covariates in linear and logistic regression models as well as potential determinants of PA engagement.

AGE

Age was divided into five categories: 18-24, 25-29, 30-34, 45-39, and 40-44.

RACE/ETHNICITY

Race/ethnicity was categorized into eight groups: Caucasian, African American, Asian, Native American/Alaskan, Pacific Islander/Hawaiian, Hispanic, and Other.

EDUCATION LEVEL

Four levels of education were created: 'less than high school', 'completed high school', 'some college or technical school', and 'graduated college or technical school'.

NUMBER OF CHILDREN IN HOUSELHOLD

Four levels of child household count were created: 'no children', 'one to three children', and 'four or more children'.

ALCOHOL CONSUMPTION

Alcohol consumption was derived from the following questions:

11.1 During the past 30 days, how many days per week or per month did you have at least one drink of any alcoholic beverage such as beer, wine, a malt beverage or liquor?

11.2 One drink is equivalent to a 12-ounce beer, a 5-ounce glass of wine, or a drink with one shot of liquor. During the past 30 days, on the days when you drank, about how many drinks did you drink on the average? NOTE: A 40 ounce beer would count as 3 drinks, or a cocktail drink with 2 shots would count as 2 drinks.

11.3 Considering all types of alcoholic beverages, how many times during the past 30 days did you have X [CATI NOTE: X = 5 FOR MEN, X = 4 FOR WOMEN] or more drinks on an occasion?

11.4 During the past 30 days, what is the largest number of drinks you had on any occasion?

Alcohol consumption was categorized into three levels: 'no alcohol', 'moderate alcohol consumption'(no more than 1 drink a day or 7 drinks a week), or 'heavy alcohol consumption'(more than 1 drink a day or more than 7 drinks a week).

SMOKING STATUS

Smoking status was divided into three categories: 'never-smoker', 'former smoker', and 'current smoker'.

DATA ANALYSIS

Data was managed using SAS version 9.4 (5). Variables of interest were re-coded or created and missing data points eliminated. Procedures were conducted, accounting for the complex sample design and weighting. Frequency procedures (PROC SURVEYFREQ) were used to obtain proportions for sample characteristics. Chi-square (X^2) tests for equal proportions were used to check for statistical significance (P \leq 0.05). Additional analysis included proportion estimates of DRS and PA by interview year as well as subgroup analysis of the MSA variable in women who met the AA recommendation. The univariate procedure (PROC UNIVARIATE) was used to check for normality and provide medians for the continuous AA variable.

Linear regression was performed (PROC SURVEYREG) to obtain beta regression estimates (β) for AA in HRD and DM groups (ND referent). Three models were created: crude, age-adjusted, and fully adjusted for all covariates.

Separate logistic regression procedures (PROC SURVEYLOGISTIC) were performed to obtain odds ratios (ORs) and 95% confidence intervals (CIs) for meeting AA, MSA, both, and neither 2008 DHHS recommendation according to DRS (ND referent group). Crude, ageadjusted, and fully adjusted models, including all covariates, were constructed for each of the four outcome variables.

For identification of significant determinants of PA, the covariates in each of the four fully adjusted logistic models were examined individually by their standardized beta coefficients (STB), which were obtained by adding the STB modification to the model statements. By taking the absolute value of the STBs with significant P values ≤ 0.05 , covariates could be ranked as determinants by their contributions to the model.

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Chapter Four: Diabetes Risk Status and Physical Activity in Pregnancy: U.S. BRFSS 2011, 2013, 2015, 2017

ABSTRACT

- *Objectives* We sought to examine differences in aerobic activity (AA) and muscle strengthening activity (MSA) by diabetes risk status (DRS) among pregnant women in the United States.
- **Background** Pregnant women without complications are advised to engage in PA to mitigate adverse outcomes. Differences may exist among parous women of diverging diabetes histories in meeting national PA recommendations.
- Methods The sample (n=9,597) included pregnant women ages 18-44, who participated in the 2011, 2013, 2015, and 2017 Behavioral Risk Factor Surveillance System. Levels for DRS were: no diabetes (ND), high risk for diabetes (HRD) due to self-reported gestational diabetes or pre-diabetes, and overt diabetes (DM). Odds ratios (ORs) for meeting PA recommendations were obtained. Covariates included age, race, education, household child count, alcohol consumption, and smoking status.
- **Results** Findings revealed that on average, group DM had 46.5 fewer minutes of weekly AA compared to group ND. Furthermore, a significantly lower OR (0.39; P<0.05) for meeting both recommendations in group DM (referent ND) was observed after adjustments.
- Conclusions We observed pregnant women with overt diabetes have lower likelihood of engaging in PA, while group HRD was similar in their PA engagement as group ND. Differences in demographic variables may contribute to PA outcomes and strategies in bridging the gap between socioeconomic status and PA engagement in pregnancy should be explored.

INTRODUCTION

Hyperglycemia generally refers to the presence of higher than normal glucose levels in the blood (1). In pregnancy, hyperglycemia may be due to chronic conditions such as type 2 diabetes mellitus (T2DM), prediabetes (PD), and gestational diabetes mellitus (GDM). These three manifestations of hyperglycemia differ in their diagnostic criteria and severity (1). The United States (U.S.) prevalence of T2DM and PD in women has increased by at least two percentage points from 1999-2012, climbing to 13.8% and 35.9%, respectively (2). The estimated prevalence of GDM in the U.S., based on data from the 2007-2014 National Health and Nutrition Examination Survey (NHANES) is 7.6% (3).

A T2DM diagnosis can be confirmed by: fasting plasma glucose (PG) \geq 126 mg/dl, a two-hour (2-H) PG \geq 200 mg/dl after a 75 g glucose load during oral glucose tolerance test (OGTT), or a glycohemoglobin (A1C) \geq 6.5% (4). Accurate diagnosis requires at least two separate positive readings for the same test. In addition, one instance of classic symptoms of hyperglycemic crisis with a random PG \geq 200 mg/dl may confirm diagnosis (4). Type 2 diabetes diagnosis heightens the risk for blindness, kidney failure, lower limb amputations, cardiovascular events, and complications in pregnancy (5). Type 2 diabetes has also been shown to augment risk for cardiovascular diseases (CVD) (6).

Prediabetes diagnosis is like that of T2DM, modified with lower cut points: fasting PG 100-125 mg/dL, 2-H OGTT 140-199 mg/dL after a 75g glucose load, and A1C 5.7-6.4% (1). Not unlike T2DM, PD carries a greater risk of damage to the eyes, kidneys, blood vessels, and heart (7). Furthermore, 5-10% of patients with PD progress to T2DM annually (8). In order to prevent disease progression, first line treatment includes: weight loss of 5-10% of body weight and 30 minutes a day of moderate intensity physical activity (PA) (8,9).

Gestational diabetes initiates in pregnancy and resolves after delivery (2). Diagnosis is often based on a 3-H 100g OGTT. Diagnosis is confirmed by two or more of: a fasting PG 95-125 mg/dl, 1-H PG \geq 180 mg/dl, a 2-H PG 155-199 mg/dl, and a 3-H PG 140-199 mg/dl (10). However, screening methods and diagnostic criteria have varied across years and governing bodies (11). This has led to varying prevalence estimates and uncertainty for patients who may not have received GDM diagnosis in previous years (12). Although GDM is not a lifelong disease, it is associated with over a seven-fold risk for T2DM (13) and a 50% increased risk for CVD (14). Maternal and fetal sequelae of GDM include increased perinatal mortality, fetal macrosomia, neonatal hypoglycemia, cesarean section, and postpartum depression (15). Furthermore, glucose intolerance, T2DM, and obesity risk are heightened in GDM offspring (16).

Physical activity has been shown to restore insulin sensitivity and minimize impaired glucose tolerance in pregnancy (17). A meta-analysis of 40 observational studies reported a 30% reduction in GDM risk for any general inclusion of PA (18). Exercise can positively impact fetal body composition with an overall increase in fetal weight and decrease in percent of fetal mass. This is due to improved maternal glucose control, improved maternal autonomic control, improved placental oxidative stress, and placental efficiency (19).

All U.S. adults without contraindications to exercise, are advised by the Department of Health and Human Services (DHHS) to stay active (20). The 2008 PA guidelines for adults recommended either 150 minutes of moderate aerobic activity (AA) or 75 minutes of vigorous AA and two days of muscle strengthening activities (MSA) per week. Aerobic activity may be completed in a minimum of 10-minute bouts (21). The new 2018 PA Guidelines for adults are comparable to the previous guidelines modified to allow AA bout duration minimums of 2 minutes (20).

Due to their unique medical considerations, pregnant women have separate recommendations for PA. Current recommendations made by the American College of Obstetricians and Gynecologists (ACOG) in 2020 state that exercise and/or PA is beneficial for most pregnant women but modifications in exercises may be necessary to account for physiological and anatomical changes (22). Pregnant women should be thoroughly evaluated by an obstetrician-gynecologist before PA recommendations are made to ensure the patient does not have medical contraindications. Women with uncomplicated pregnancies should be encouraged to engage in aerobic and muscle strengthening activities (MSA) before, during, and after pregnancy. Furthermore, activity restriction should not be routinely prescribed as a treatment to reduce preterm birth (22).

The 2008 and more recent 2018 U.S. DHHS guidelines on PA in pregnancy recommend at least 150 minutes of moderate-intensity AA per week, avoiding supine position and high fall risk sports such as horseback riding (20,21). Similarly, the 2019 Canadian guidelines recommend 150 minutes of moderate-intensity aerobic activity (AA) per week, a minimum of three days per week (23). In addition, Canadian guidelines encourage incorporation of a variety of aerobic and resistance exercise in addition to yoga, stretching, and pelvic floor muscle training (23). Although no set dose of MSA has been established for pregnant women, resistance exercise is encouraged by governing pregnancy experts.

Despite the overwhelming evidence of benefits (24), less than 15% of women achieve the minimum recommendation of 150 minutes of moderate intensity PA per week during pregnancy (25). About one third of pregnant women do not engage in any PA (26). Understanding the

various factors, which may contribute to PA engagement or lack thereof is necessary to create effective interventions.

Barriers to PA engagement have been studied, including knowledge gaps regarding sports and exercise and perceived inconvenience (27). Based on a 2017 review of qualitative and quantitative evidence, among the most prominent barriers to exercise in pregnancy were: lack of time due to work, tiredness, pregnancy-related symptoms, and lack of social support (28). Furthermore, there remains prevailing uncertainty among patients and clinical providers concerning the risk of miscarriage, growth restriction, preterm birth, fatigue, or harm to the fetus (28).

Though we know that PA recommendations in pregnancy are infrequently met, sparse information exists on how self-reported GDM and PD histories compare with self-reported diabetes and euglycemia in meeting AA recommendations and two days of MSA per week. This study will examine the differences in PA engagement for parous women with varied diabetes risk status (DRS). Therefore, the study aims to answer three questions: 1) Is there an association between DRS and meeting the 2008 DHHS PA recommendation in pregnancy? 2) Is there an association between DRS and engaging in at least two days of MSA per week in pregnancy? 3) Are there other major determinants that are associated with meeting the recommendations and two days of MSA in pregnancy?

METHODS

SAMPLE POPULATION

The data comes from the 2011, 2013, 2015, and 2017 Behavioral Risk Factor Surveillance System (BRFSS), a population-based survey administered through random-digitdialed landline and cellular telephones. The BRFSS obtains information on participant demographics, health behaviors, and health related issues. Data is collected on the noninstitutionalized U.S. civilian population in all 50 states, the District of Columbia, and three U.S. territories. Sections were stratified according to state regions and within each stratum are randomized cluster units (households). The raking method for sample weighting was used to ensure appropriate representation of demographic variables. Participants are pregnant women between the ages of 18 and 44 who completed all relevant sections of the BRFSS. Women who reported a diabetes diagnosis at age 5 or younger were excluded, as they were likely to have type 1 diabetes. After excluding incomplete responses and probable type 1 diabetes (n=1,482), there was a total of 9,597 participants.

EXPOSURE

To obtain the independent variable, DRS, participants were asked if they had ever been told by a doctor that they had diabetes and whether it was only when they were pregnant. Women reporting "yes" to this question were given diabetes status. Those who reported diabetes only in pregnancy or prediabetes were classified as GDM and PDM, respectively, and considered at a high risk for T2DM. Those who reported having no diabetes were considered to have nondiabetes status. Therefore, three DRS groups were established: high risk for diabetes (HRD; n=457), no diabetes (ND; n=9036), and diabetes (DM; n=104).

OUTCOME

The dependent variables in this study were engaging in AA, MSA, both, and neither recommendations based on the 2008 DHHS guidelines. To obtain the AA variable, participants were asked about the type, frequency, and duration of weekly PA performed in the past month. Depending on the intensity and total minutes of AA, participants either met or did not meet the AA guidelines. Additionally, minutes of AA were examined as a continuous variable. The frequency of MSA was obtained by participants being asked the question: "During the past month, how many times per week or per month did you do physical activities or exercises to strengthen your muscles?" Depending on the frequency of MSA (less than two times per week or at least two times per week), participants either met or did not meet the MSA guidelines.

COVARIATES

Covariates included in the analysis were age, race, level of education completed, number of children in the household, alcohol consumption, and smoking status. Age was divided into five categories (18-24, 25-29, 30-34, 35-39, and 40-44). Race was categorized into eight groups: Caucasian, African American, Asian, Native American/Alaskan, Pacific Islander/Hawaiian, Hispanic, and Other. Education level was categorized into 'less than high school', 'completed high school', 'some college or technical school', and 'graduated college or technical school'. Number of children in the household was sectioned into 'no children', 'one to three children', and 'four or more children'. Alcohol consumption was reported based on the past 30 days prior to completion of the survey and categorized as 'no alcohol consumption', 'moderate alcohol consumption' (no more than 1 drink a day or 7 drinks a week), or 'heavy alcohol consumption' (more than 1 drink a day or 7 drinks a week). Smoking status was categorized as 'non-smoker', 'previous smoker', or 'current smoker'.

STATISTICAL ANALYSIS

Data was analyzed with SAS version 9.4. Variables of interest were re-coded, and prevalence estimates were stratified by DRS using PROC SURVEYFREQ. All procedures included the sample weight, strata, and cluster variables to account for the complex stratified sampling design of BRFSS. PROC SURVEYMEANS was used to determine mean frequencies for continuous variables. Chi-square (χ^2) tests for equal proportions were used to check for statistical significance (P≤0.05). Normality was checked and medians obtained with PROC UNIVARIATE.

Beta estimates (β) for the continuous AA variable were obtained using the SURVEYREG procedure. All variables were then converted to categorical or dichotomous, with aerobic PA, MSA, both, and neither dichotomized into "meets recommendations" or "does not meet recommendations". The SURVEYLOGISTIC procedure allowed for attainment of odds ratios (ORs) and 95% confidence intervals (CI) related to the proposed research questions. Furthermore, standardized beta coefficients (STB) were produced. By examining the absolute

value of the STB and the P-value for statistical significance, covariates from the final model were ranked as determinants for each outcome.

RESULTS

Table 1 illustrates proportions for sample population characteristics in the total sample and stratified by DRS. Statistically significant variance in distributions between DRS categories are observed for age, number of children in the household, and alcohol consumption. Apart from meeting the MSA recommendation, Table 2 illustrates the general pattern of decreasing prevalence of PA from ND to HRD to DM.

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DKI 55 2011, 2013, 2017					
	Total	ND	HRD	DM	χ^2 Test
	N (Weighted%)				Р
Total	N=9597	9036 (94.3)	457 (4.8)	104 (0.9)	
Age					<.0001
18-24	2113 (28.8)	2033 (29.7)	53 (11.6)	27 (31.7)	
25-29	2713 (27.2)	2592 (27.3)	96 (25.5)	25 (23.1)	
30-34	2873 (27.9)	2688 (27.5)	162 (37.0)	23 (22.5)	
35-39	1485 (12.4)	1351 (12.0)	115 (19.8)	19 (14.1)	
40-44	413 (3.7)	372 (3.5)	31 (6.1)	10 (8.6)	
Race/Ethnicity					0.1571
White	6203 (51.7)	5882 (52.0)	269 (46.1)	52 (54.8)	
African American	825 (12.9)	779 (13.1)	34 (8.2)	12 (10.8)	
Native American/Alaskan	242 (1.3)	224 (1.3)	14 (0.9)	4 (0.6)	
Asian	342 (5.9)	317 (5.7)	21 (8.8)	4 (8.6)	
Native Hawaiian/ Pacific Islander	88 (0.3)	78 (0.2)	7 (0.8)	3 (0.5)	
Hispanic	1584 (26.0)	1463 (25.6)	96 (33.0)	25 (21.2)	
Other	313 (1.9)	293 (1.9)	16 (2.1)	4 (3.4)	
Education Level					0.1948
Did not complete HS	777 (16.2)	710 (15.8)	56 (22.9)	11 (15.4)	
Completed HS	2176 (24.2)	2030 (24.1)	113 (26.1)	33 (27.9)	
Some college/technical school	2553(28.9)	2403 (29.2)	122 (24.8)	28 (22.7)	
Graduated college/technical	4091 (30.7)	3893 (30.9)	166 (26.1)	32 (34.0)	
school					
Household					0.0024
None	2981 (33.1)	2862 (33.8)	87 (19.8)	32 (38.5)	
1-3 children	5979 (60.2)	5594 (59.7)	324 (72.0)	61 (51.4)	
4 or more	637 (6.6)	580 (6.5)	46 (8.2)	11 (10.1)	
Alcohol Consumption (Based					< 0001
on the past 30 days)	9606 (99.9)	2001 (22 ()	420 (02 5)	96 (79 4)	\$.0001
None	8000 (88.8)	8091 (88.0)	429 (93.3)	80 (78.4)	
Moderate	883 (9.2)	848 (10.0)	23(5.2)	12(14.8)	
Heavy	108 (1.1)	97 (1.4)	5 (1.3)	6 (6.8)	
Smoking Status		(200 (71 7)	202 ((4.0)		0.1091
Never smoker	6/58 (70.3)	0398 (71.7)	292 (64.9)	68 (68.0)	
Former smoker	2012 (21.0)	1864 (19.6)	126 (27.7)	22 (20.1)	
Current smoker	827 (8.7)	774 (7.3)	39 (7.4)	14 (11.9)	

Table 1. Characteristics of Pregnant Women by Diabetes Risk Status:BRFSS 2011, 2013, 2015, 2017

BRFSS: Behavioral Risk Factor Surveillance System; ND: no diabetes; HRD: high-risk for diabetes due to selfreported gestational diabetes or prediabetes; DM: overt diabetes; HS: high school; level of significance set to P≤0.05

Diabetes Status	No AA	No MSA	Meets AA Rec ^a	Meets MSA Rec ^b	Meets Both Recs ^c	Meets Neither ^d		
		n (weighted %)						
ND	2525	6265	3709	1681	1087	4733		
N=9036	(27.9%)	(69.3%)	(39.2%)	(16.9%)	(10.9%)	(54.8%)		
HRD	150	358	182	60	42	257		
N=457	(32.8%)	(78.3%)	(39.2%)	(15.7%)	(10.5%)	(55.6%)		
DM N=104	65 (62.5%)	80 (76.9%)	36 (30.1%)	13 (17.9%)	7 (5.0%)	62 (57.0%)		
Total	2720	6674	3927	1754	1135	5052		
N=9597	(28.3%)	(69.5%)	(39.2%)	(16.8%)	(10.8%)	(54.8%)		

Table 2. Prevalence Estimates for Physical Activity According to Diabetes Risk Status: BRFSS 2011, 2013, 2015, 2017

BRFSS: Behavioral Risk Factor Surveillance System; ND: no diabetes; HRD: high-risk for diabetes due to selfreported gestational diabetes or prediabetes; DM: overt diabetes; AA: aerobic activity; MSA: muscle strengthening activity; ^a2008 Department of Health and Human Services (DHHS) recommendation of 150 minutes of moderate intensity AA/wk.^b2008 DHHS recommendation of 2 days/wk of MSA. ^cboth "a" and "b"; ^dneither "a" nor "b"; level of significance set to P≤0.05; Variance in distributions were statistically significant (P<0.05) for all measures.

DIFFERENCES IN AEROBIC ACTIVITY BY DIABETES RISK STATUS

Table 3 provides β values for minutes of AA per week in the HRD and DM groups (ND referent) for crude, age adjusted, and fully adjusted models. There was a non-normal distribution for the continuous AA variable, but the sample size was large enough to allow for linear regression without violations. On average, those with diabetes had 46.5 fewer minutes in AA compared to those with no diabetes. Having GDM or PD contributes modestly to the likelihood of engaging in AA when compared to having no diabetes.

	HRD	DM
Model	β (SE)	β (SE)
Crude	-23.6 (0.041)	-45.9 (0.041)
Age Adjusted	-22.2 (0.036)	-43.4 (0.320)
Fully Adjusted ^a	-2.51 (0.078)	-46.5 (0.078)

Table 3. Linear Regression for Aerobic Activity in per Week in Pregnancy by Diabetes RiskStatus

^aAccounts for age, race/ethnicity, education level, number of children in the household, alcohol consumption, and smoking; β : beta regression estimate; HRD: high risk for diabetes due to self-reported gestational diabetes or prediabetes; DM: overt diabetes; SE:standard error P<0.0001 level of significance for all values listed

ODDS RATIOS FOR PHYSICAL ACTIVITY

Table 4 represents odds of meeting AA, MSA, both, and neither 2008 DHHS recommendations. After adjustments, the odds of meeting both AA and MSA recommendations were approximately 60% lower in the DM group (ND referent; OR 0.39; CI 0.19-0.82). No other statistically significant relationship between DRS and PA recommendations was observed.

MUSCLE STRENGTHENING ACTIVITY DIFFERENCES

Interestingly, although the odds of meeting both recommendations were significantly lower in group DM (Table 4), the prevalence of MSA was slightly higher (Table 2). Not illustrated are the median number of days of MSA per week in women reporting at least one day of MSA in the past 30 days: 2.00, 2.00, and 1.00 in groups ND, HRD, and DM, respectively. Table 5 exhibits results from a subgroup analysis limited to only women who met the AA recommendations to determine whether the DM subgroup differ in meeting the MSA recommendations when compared to the ND and HRD subgroups. Although not statistically significant (P=0.3382), the percentage of meeting the MSA recommendations (16.5% SE 6.0%) was lower than ND and HRD percentages (27.8% and 26.9%, respectively).

 Table 4. Odds Ratios for Meeting Physical Activity Recommendations by Diabetes Risk

 Status

		Meets AA	Meets MSA	Meets Both	Meets Neither
Crude	HRD	OR=0.96 CI=0.66-1.40	OR=1.00 CI=-0.58-1.72	OR=0.96 CI=0.44-2.08	OR=1.03 CI=0.72-1.49
	DM	OR=1.02 CI=0.53-1.95	OR=0.36 CI=0.11-1.12	OR=0.43* CI=0.2-0.91	OR=1.09 CI=0.64-1.86
Age- adjusted	HRD	OR=1.01 CI=0.70-1.48	OR=1.09 CI=0.60-1.98	OR=0.96 CI=0.44-2.10	OR=1.02 CI=0.71-1.47
	DM	OR=0.67 CI=0.39-1.17	OR=0.93 CI=0.44-1.99	OR=0.43* CI=0.20-0.92	OR=1.08 CI=0.64-1.8
Fully adjusted ^a	HRD	OR=1.07 CI=0.72-1.59	OR=1.15 CI=0.66-2.00	OR=1.23 CI=0.58-2.60	OR=0.93 CI=0.64-1.36
	DM	OR=0.64 CI=0.37-1.11	OR=1.00 CI=0.45-2.23	OR=0.39* CI=0.19-0.82	OR=1.15 CI=0.68-1.95

*P<0.05 level of significance; ^aAdjusted for age, race/ethnicity, education level, number of children in household, alcohol consumption, and smoking status; AA: aerobic activity; MSA: muscle strengthening activity; ^a2008 Department of Health and Human Services (DHHS) recommendation of 150 minutes of moderate intensity AA/wk.^b2008 DHHS recommendation of 2 days/wk of MSA. ^cboth "a" and "b"; ^dneither "a" nor "b"; HRD: high risk for diabetes due to self-reported gestational diabetes or prediabetes; DM: overt diabetes Referent group: no diabetes

those who Meet the AA [®] Recommendation			
	ND	HRD	DM
n	1087	42	7
Percent	27.8	26.9	16.5
Standard Error	1.2	7.9	6.0

 Table 5. Proportions of Pregnant Women Meeting the MSA^a Recommendations Among those who Meet the AA^b Recommendation

 $P Value^* = 0.3382$

*P value derived from Wald Chi-Square Test; ^a2008 Department of Health and Human Services (DHHS) recommendation of 2 days/wk of muscle strengthening activity; ^b2008 DHHS recommendation of 150 minutes of moderate intensity aerobic activity/wk; ND: no diabetes; HRD: high risk for diabetes due to self-reported gestational diabetes or prediabetes; DM: overt diabetes

DETERMINANTS OF PHYSICAL ACTIVITY

Table 6 describes the top three determinants associated with the odds of meeting the 2008 DHHS recommendations. The odds of meeting the AA recommendation were predominantly negatively influenced by self-reported African American, Hispanic, or Asian race. The odds of meeting the MSA recommendation were positively impacted by consuming alcohol in the past 30 days and completing more than high school and negatively impacted by having 1-3 children at home. The odds of meeting both and neither recommendations were highly influenced by a combination of the top three AA and MSA determinants.

PA Recommendation	Determinant	STB	P value
AA ^a			
1	African American	-1.28	< 0.0001
2	Hispanic	-1.16	0.0015
3	Asian	-1.08	0.0043
MSA ^b			
1	Consumed Alcohol in Past 30 Days	2.00	< 0.0001
2	Completed > HS	1.90	0.0002
3	1-3 Children at Home	-1.62	< 0.0001
Both ^c			
1	1-3 Children at Home	-1.97	< 0.0001
2	Consumed Alcohol in Past 30 Days	1.75	< 0.0001
3	African American	-1.58	0.016
Neither ^d			
1	Consumed Alcohol in Past 30 Days	-1.40	< 0.0001
2	Hispanic	1.37	0.0001
3	African American	1.26	< 0.0001

Table 6. Top Three Determinants of Meeting AA and MSA Recommendations

HS: High School; PA: physical activity; AA: aerobic activity; MSA: muscle strengthening activity; ^a2008 Department of Health and Human Services (DHHS) recommendation of 150 minutes of moderate intensity AA/wk.^b2008 DHHS recommendation of 2 days/wk of MSA. ^c both "a" and "b"; ^d neither "a" nor "b"; STB: Standardized beta coefficient; All variables included in the model were diabetes risk status, age, race, education level, number of children in household, alcohol consumption, and smoking status

TRENDS OF PHYSICAL ACTIVITY AND DIABETES RISK STATUS: 2011-2017

From Table 7, we can see no statistically significant change in meeting 2008 DHHS PA

recommendations (P>0.05) across BRFSS interview years. However, the slight and consistent

uptrend in MSA, from 15% in 2011 to 19% in 2017, should be noted. Furthermore, no

significance was seen in distribution of DRS in pregnancy by interview year (Figure 1), although

a five-fold increase in overt diabetes prevalence from 2011 to 2017 may be observed.

Year n	2011 (n=2773)	2013 (n=2638)	2015 (n=2031)	2017 (n=2155)	χ ² Test
Recommendation	n (%)	n (%)	n (%)	n (%)	P- Value
AA ^a	1122 (39.9)	1056 (38.1)	855 (37.8)	894 (40.7)	0.5954
MSA ^b	438 (15.0)	469 (15.5)	403 (17.8)	444 (19.0)	0.1061
Both ^c	284 (10.1)	295(9.8)	267 (11.6)	290 (11.7)	0.5129

Table 7. Prevalence of Meeting PA Recommendations in Pregnancy by Year

Percentages are weighted; ; ^a2008 Department of Health and Human Services (DHHS) recommendation of 150 minutes of moderate intensity AA/wk.^b2008 DHHS recommendation of 2 days/wk of MSA. ^cboth "a" and "b"



Figure 1. Trends in Prevalence of Overt Diabetes and High-Risk for Overt Diabetes in Pregnancy: BRFSS 2011-2017

Percentages are weighted.

DISCUSSION

This study combines GDM and PD together as one high-risk for diabetes group. Though secondary to diabetes, both GDM and PD carry gravid and post-gravid health threats (7,13-16). Given the relatively small numbers of self-reported pregnancy in our study population, and even lower prevalence of hyperglycemic pregnancies, we combined four recent survey years of BRFSS data in an attempt to acquire enough power to examine our associations of interest.

Lack of statistical significance in odds of meeting individual AA and MSA recommendations may be due to the overall diminished PA engagement in pregnancy (29), attenuating differences among DRS groups. Furthermore, relatively small sample sizes for DM

and HRD groups may have contributed to a loss of statistical power to accurately demonstrate some relationships. With regards to meeting the AA guidelines, our study found no significant differences in ORs after adjusting for covariates in the fourth model. This mirrors previous findings from a 2003 BRFSS study examining nonpregnant women ages 18-44 (n=4718), with and without a history of GDM where there was no difference in meeting the AA guidelines between groups after adjusting for age, race, education level, current employment, marital status, presence of children in household, smoking status, self-rated health, and BMI.

Markedly observed in this study is the inverse association of overt diabetes and meeting both AA and MSA recommendations. This finding is reflective of a BRFSS study on nonpregnant women, reporting that non-pregnant women of a childbearing age with current diabetes are 40% more likely to fail to meet LTPA their recommendations compared with their non-diabetes counterparts (P<0.05).

Top determinants for odds of meeting the U.S. DHHS PA guidelines for adults closely mirrored differences in sample population characteristics. African American, Hispanic, and Asian race/ethnicities negatively influenced the odds of meeting AA recommendations. Although there was no significance in the distribution (P=0.1571), there may be intra-variability in these race/ethnicity categories. Specifically, 33% of the HRD group was Hispanic compared to 26% of the ND group and 21% of the DM group. Published evidence has identified Hispanic minority as major demographic risk factor for GDM, a large portion of the HRD group (16). Furthermore, being part an ethnic minority is associated with higher diabetes prevalence (30).

We found that completing more than high school positively impacted the odds of meeting the MSA recommendations while lower education level has been identified as a predictor for T2DM (30). Having 1-3 children significantly contributed to higher odds of MSA. Having four or more children was not a top determinant, most likely due to insufficient cell size. Future studies may consider using a broader "one or more children" category. Such dichotomization was used in a 2001-2003 BRFSS study that observed a higher prevalence of having at least one child in women with GDM (~87% vs ~66% in no GDM group; p<0.01). Furthermore, having GDM and at least one child living at home were associated with compromised healthy lifestyle behaviors (9).

Given the widespread discouragement of alcohol consumption in pregnancy and deleterious effects of alcohol on fetal development (31), the strong positive influence of alcohol consumption on odds of meeting MSA and both recommendations in pregnancy seem peculiar. However, alcohol consumption has been observed to favorably improve the odds of meeting MSA guidelines in adults with dyslipidemia and augmented waist circumference (32). In another study examining the relationship between alcohol consumption and metabolic syndrome in adults, moderate and above moderate alcohol consumption was positively associated with improved metabolic factors, including decreased PG levels (33). More research is needed to understand this relationship outside of pregnancy. However, existing evidence on the harmful effects of alcohol exposure on the fetus still warrant caution during pregnancy (31)

This study was not without its limitations. The cross-sectional nature of BRFSS does not allow us to infer causality. According to a 2015 CDC report, 31.1% of all U.S. women have PDM but only 14.1% are aware of their disease state (34). Since our study relied on self-report, we may have mistakenly classified a large percentage of high-risk women as normal, which may have buffered the true influence of diabetes status on PA participation. Variables that may provide additional information when accounting for risk that were not included in the survey include pre-pregnancy BMI, specific diabetes subtypes, pre-conception care, and contraindications to exercise. In particular, the lack of information on gestational age hindered us from identifying women that may be overweight or obese and whether they were far enough along to be eligible for GDM screening/diagnosis. Furthermore, the study sample size did not allow examination of determinants of PA by DRS, due to unstable cell sizes.

Although MSA recommendations are not specified in the 2018 DHHS guidelines for pregnant women, we opted to include the MSA guidelines of two days of MSA per week in the general adult population. Strength training needs greater emphasis due to its role in diabetes prevention. In a prospective cohort study (35), resistance exercise and lower intensity MSA were both associated with a lower risk of T2DM in the pooled analysis. Greater glycemic load increased with greater volume of MSA, suggesting improved insulin sensitivity with this mode of activity (35). Resistance training has also been shown to improve feelings of fatigue associated with pregnancy (36,37).

Preconception counseling, with PA included, is recommended by the ADA (38).Clinical recommendations for promoting exercise in pregnant women with PD, GDM, and T2DM have been established (22,39). However, many women with diabetes are not meeting with clinical providers to receive prenatal counseling (40). Moreover, cognitive dissonance may exist regarding healthy lifestyle and other lifestyle factors. Several strategies to increase PA participation in pregnancy have been proposed. In a systematic review examining behavior change interventions, goals and planning with feedback was found to be the most effective behavior change technique (41). Other interventions based on social support and self-efficacy have also proven effective (42,43). Interventions specifically targeting aspects of SES disadvantage may prove efficacious, as women at socioeconomic disadvantage are less likely to meet LTPA guidelines (44).

Furthermore, women in general may not be receiving quality counseling by their physicians on exercise in pregnancy (45, 46) It is essential that pregnant women are advised to exercise by their physicians as they will be more likely to engage in PA (47). Increased education by healthcare providers may also ameliorate feelings of uncertainty among certain women. Feeling unsafe/unsure about moderate PA may be associated with non-White race/ethnicity, low education, low income, and not participating in moderate PA with no intention to start exercising (48).

CONCLUSION

Pregnancy is an opportunity for clinicians to encourage healthy lifestyle patterns, including PA. This study illuminates the health disparities associated with DRS and PA participation in pregnancy. Future studies should examine PA prevalence using objective measures of PA participation, hyperglycemia, and clinical assessment of participants. Ultimately, increased efforts should be made for interventions targeted at improving health outcomes by breaching the gaps in regular AA and MSA participation during pregnancy for women with DM, and characteristics such as multiple children, lower education, and/or racial/ethnic minority backgrounds, improving health outcomes.

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Appendix A



DATE:	April 30, 2020
<u>TO:</u>	Ms. Bethany Rand
<u>VIA</u> :	Dr. James Churilla, PhD
DEPT:	Clinical and Applied Movement Sciences
FROM:	Dr. Jennifer Wesely, Chairperson UNF Institutional Review Board
<u>RE:</u>	Review conducted on behalf of the UNF Institutional Review Board "Diabetes Risk Status and Physical Activity in Pregnant Women: BRFSS 2011, 2013, 2015, 2017"

This is to advise you that your project, "Diabetes Risk Status and Physical Activity in Pregnant Women: BRFSS 2011, 2013, 2015, 2017," was reviewed on behalf of the UNF Institutional Review Board and was declared "not research involving human subjects" based on the definitions provided in the U.S. Department of Health and Human Services Code of Federal Regulations found at 45 CFR 46.102. As such, this project qualifies for a Waiver of IRB Review.

Please note, this waiver does not absolve the Principal Investigator from complying with other federal, state, or local laws or institutional policies and procedures that may be applicable in the conduct of this project.

This waiver applies to your project in the form and content as submitted to the IRB for review. Any variations or modifications to this project involving the participation of human subjects must be approved by the IRB prior to implementing such changes. Please maintain a copy of this waiver for your records.

Thank you for submitting your project to the IRB for consideration. Should you have any questions or if we can be of further assistance, please contact the Research Integrity office at 904-620-2455, or IRB@unf.edu.

IRB Form Version 01.03.2019

Appendix B

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EXTERNAL COMMITTEE MEMBER FORM

Instructions: Use this form to nominate a non-UNF faculty member to serve on a thesis/dissertation committee. This form must be completed by the department and forwarded to the Graduate School for approval. A copy of the nominee's CV must be attached.

During the graduation term, if this form is required, please be sure the form is on file by the posted deadline (https://www.unf.edu/graduateschool/student resources/Thesis and Dissertation Procedures.aspx).

Student N#: Redacted

Student Full Name: Bethang G. hand

Nominated Committee Member's Name: <u>SAMAN tha</u> Ehrlich, Ih. D. MPH Department/College Recommending: <u>CAMS / Brook's (Alege of Health</u> Graduate Program Recommending: <u>EVERUSE Science and Chronic</u> PISEASE

Nominated committee member's highest degree earned, where earned, and discipline: <u>Bstdoctoral fellow</u>, Kaller Permanente Northeyn Califernia Division of Research, Nomen's 4Children's hearth, doctoral degree in Epidemichey, VC Berkeles If a Ph.D. is not the usual terminal degree required to sit on a thesis/dissertation committee in this field, provide the control of the

degree that is appropriate: _____

If the nominated committee member does not have the appropriate terminal degree required to serve as a member of a committee, please list the credentials or experiences that would qualify him/her to sit as a committee member:

Has the nominated committee member served on a committee at UNF before?
Yes No

If so, please specifiy the committee:

CERTIFICATION

The undersigned certify that they have reviewed the credentials of the nominee and requests approval. A copy of the nominee's QV must be attached. Redacted 12/3/16

Redacted

Program Director Signature

GRADUATE SCHOOL

□ Approved Comments: □ Disapproved

Graduate School Dean Signature

Date

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childhood risk factors

The Graduate School

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Student N#: Redacted
Student Full Name: Bethany G. Rand
Lamer Durank Dh D M Sr MS
Nominated Committee Member's Name: Jan De Var Min (Jan
Department/College Recommending: CAMS/Brooks Callege at flatth
Graduate Program Recommending: EXEVCISE SCIENCE and Chronic USCODE Indiana University
Nominated committee member's highest degree earned, where earned, and discipline: <u>th.D.</u> Maria VIIVASITY Human Performance (Exercise Physiology)
If a Ph.D. is not the usual terminal degree required to sit on a thesis/dissertation committee in this field, provide the degree that is appropriate:
If the nominated committee member does not have the appropriate terminal degree required to serve as a member of a committee, please list the credentials or experiences that would qualify him/her to sit as a committee member:
If so, please specifiy the committee:
The undersigned certify that they have reviewed the credentials of the nominee and requests approval. A copy of the
Redacted 12/3/19
Redacted Date
Program Director Signature Date
GRADUATE SCHOOL
□ Approved Comments: □ Disapproved
Graduate School Dean Signature Date

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The Graduate School

EXTERNAL COMMITTEE MEMBER FORM

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During the graduation term, if this form is required, please be sure the form is on file by the posted deadline (https://www.unf.edu/graduateschool/student resources/Thesis and Dissertation Procedures.aspx).

Student N#: Redacted

Student Full Name: Bethany G. Hand

Nominated Committee Member's Name: LAUVIC Wideman, Ph.D., MS Department/College Recommending: CAMS/Brooks College of Heathn Graduate Program Recommending: Exercise Science and Chronic Disease

Nominated committee member's highest degree earned, where earned, and discipline: Ph. P. in EXErcise Physiology inversity of Vilginia, the impact of exercise, disease, and injury on the endearine system

If a Ph.D. is not the usual terminal degree required to sit on a thesis/dissertation committee in this field, provide the degree that is appropriate:

If the nominated committee member does not have the appropriate terminal degree required to serve as a member of a committee, please list the credentials or experiences that would qualify him/her to sit as a committee member:

Has the nominated committee member served on a committee at UNF before? I Yes INO

If so, please specifiy the committee:

CERTIFICATION

The undersigned certify that they have reviewed the credentials of the nominee and requests approval. A copy of the nominee's Cybrust be attached.

Redacted

GRADUATE SCHOOL

□ Approved Comments: □ Disapproved

Graduate School Dean Signature

Date

Revised Jun-19

VITA

Bethany Rand is a graduate research assistant and lab instructor in the Clinical and Applied Movement Sciences Department at the University of North Florida in Jacksonville, Florida. She also completed her undergraduate coursework at the University of North Florida, where she earned a Bachelor of Science degree in Public Health.

In 2016, she began her career in the healthcare field as a Wellness Specialist for Welltality, a privately owned company that partners with general practitioners to administer Annual Wellness Visits to eligible Medicare patients. Since 2017, she has been working as Patient Care Technician in the surgical cardiovascular intensive care unit at Baptist Medical Center.

Her research studies have included examination of the associations between self-reported clinically diagnosed hyperglycemia and gravid and post-gravid physical activity in childbearing age women. Her primary focus has been on aerobic and muscle strengthening activities in women with gestational diabetes. She currently resides in Jacksonville, Florida, and plans to move to Knoxville, Tennessee to pursue a doctoral degree in Public Health.