Optimizing blood glucose control through timing of exercise in pregnant individuals diagnosed with gestational diabetes mellitus

by

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Abstract

Exercise is known to help control blood glucose values in women with gestational diabetes mellitus (GDM). Research has shown that controlling postprandial blood glucose values is key in improving glycemia and maternal/fetal health outcomes. However there is no research on the optimal timing of exercise. Exercise prescriptions that can better manage postprandial blood glucose values and can be translated into clinical practice are critically needed for women with GDM. This study was developed to investigate the optimal timing of light-to-moderate intensity exercise on postprandial and 24h blood glucose values in pregnant individuals with and without GDM. Five pregnant women with GDM and five without wore a flash glucose monitoring system for 14 days. They each completed two exercise interventions in random order. The first intervention required participants to walk for 10 minutes immediately following meals three times per day (SHORT), while the complementary condition required participants to go for one 30-minute walk each day at any time other than within the hour immediately following their meals (LONG). Both conditions occurred for a duration of 5 days with a two day washout in between, for a total of 150 mins of light to moderate intensity physical activity per week. Dietary intake and physical activity were not different between groups prior to the intervention. Fasting, 24h mean, peak, nadir glucose values and time > 7.8 mmol/L were significantly higher in the women with GDM compared to the normoglycemic group pre-intervention. There was a significant effect of group by condition whereby the GDM group had significantly higher 1 hour postprandial blood glucose values after lunch and dinner in the NORMAL and LONG condition, but not in the SHORT. Shorter, more frequent bouts of physical activity compared to one longer bout of physical activity more effectively normalize GDM 1h post-lunch and dinner glucose values to be comparable with that of a normoglycemic pregnant group. Fasting, 24h mean, and nadir glucose

values were not influenced by exercise. Both exercise conditions were effective at reducing peak glucose values and time spent > 7.8 mmol/L in women with GDM to be comparable with that of the healthy pregnant population. Results from this study may have clinical relevance and may help healthcare providers and patients better manage blood glucose values during GDM.

Key words: gestational diabetes mellitus, walking, glycemic control, pregnancy, postprandial blood glucose.

Preface

This thesis is an original work by Ly-Anh Reid. No part of this thesis has been published previously. This research project received research ethics approval from the University of Alberta Research Ethics Board on June 2 2020, under the project name: “Exercise timing in gestational diabetes mellitus” (Pro00097525).

Dr. Margie Davenport, Dr. Rshmi Khurana and I contributed to the design, acquisition, analysis, and interpretation.

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List of Abbreviations

GDM	Gestational diabetes mellitus
ACOG	American College of Obstetricians and Gynecologists
GCT	Glucose challenge test
OGTT	Oral glucose tolerance test
1hPG	1-hour plasma glucose
2hPG	2-hour plasma glucose
FPG	Fasting plasma glucose
SMBG	Self-monitoring blood glucose
CGM	Continuous glucose monitor
FGM	Flash glucose monitor
OR	Odds ratio
SD	Standard deviation
RCT	Randomized controlled trial
SMD	Standardized mean difference
BMI	Body mass index

CHAPTER 1: INTRODUCTION

Significance

Gestational Diabetes Mellitus (GDM) is defined as "glucose intolerance with onset or first recognition during pregnancy". This condition affects 4.7% of the general obstetric population in Canada, and up to 17% of women with risk factors for GDM. [1] Women diagnosed with GDM have reduced blood glucose regulation, which may contribute to an increased risk of pregnancy complications including pre-eclampsia, Caesarian section, macrosomia and neonatal hypoglycemia. [2–4] The health risks associated with GDM are amplified when blood glucose levels are poorly controlled. [1] Previous studies have suggested control of postprandial blood glucose values may be key to improving maternal and fetal health outcomes in women with GDM. [5–7]. Currently, front-line therapies include daily blood glucose monitoring, dietary modifications around carbohydrate intake, pharmacological treatment (most commonly insulin or Metformin), and recommendations for aerobic exercise. [8]

Pregnant women with GDM are advised to complete 150 minutes of moderate-intensity exercise per week. [9] Recently, the American College of Obstetrics and Gynecology (ACOG) suggested that a 10-15 minute walk after each meal has been suggested to improve glycemic control. [8] However, this recommendation is based on expert opinion and not empirical evidence. The current study will provide insight on the acute blood glucose response to the timing of daily exercise around meals in women diagnosed with GDM.

Objective

The aim of this study was to quantify changes in blood glucose control in response to postprandial versus daily exercise (outside of the 1 hour post-meal window) as well as 24-hour blood glucose control in women with and without gestational diabetes mellitus.

Delimitations

Six pregnant women diagnosed with GDM and six without who were >18 years, otherwise healthy (not diagnosed with respiratory, cardiovascular, metabolic, or neurological disorders that would influence glucose metabolism) and without absolute contraindications to prenatal exercise (e.g. preeclampsia, placenta previa after 28 weeks' gestation, incompetent cervix, uncontrolled hypertension), were recruited for a randomized cross-over controlled trial. [9] As a proxy to blood glucose levels, interstitial fluid glucose concentrations were measured through a flash glucose monitoring system in response to 1) a daily 30-minute bout of light to moderate intensity walking at any point during the day except the hour after meals and 2) three daily 10-minute bouts of light to moderate intensity walking, each bout completed in the hour following breakfast, lunch and dinner. Physical activity was monitored through an accelerometer, and participants kept a food log for food intake tracking.

Limitations

Participants took part in the study under free-living conditions. The major limitation of this design were the possible inconsistencies with adherence compared to controlled laboratory conditions. However, this design best represents everyday life, and should one of the walking conditions demonstrate superior blood glucose management, the protocol could be easily be disseminated to patient care providers and implemented into daily life.

Hypotheses

Hypothesis 1:

We hypothesised that 1hr and 2hr postprandial blood glucose values, fasting, and 24 hour glycemic control (mean, peak, time in target, time > 7.8 mmol/L, time <3.3 mmol/L) values in

women with GDM would be poorer compared to pregnant women without GDM across all conditions.

Hypothesis 2:

We hypothesised that 1hr and 2hr postprandial blood glucose values, fasting, and 24 hour glycemic control (mean, peak, time in target, time > 7.8 mmol/L) values would improve in both the GDM and NON-GDM groups due to exercise, with greater improvements in the GDM group. Time < 3.3 mmol/L would not be affected.

Hypothesis 3:

We hypothesised that in both the GDM and NON-GDM group, three 10-minute bouts of walking during the first hour after eating breakfast, lunch, and dinner would be more effective than one daily 30-minute walk (at any time other than within the hour after eating) at improving 1hr and 2hr postprandial blood glucose values, fasting values, and 24 hour glycemic control (mean, peak, time in target, time > 7.8 mmol/L) values, but would not affect time < 3.3 mmol/L.

CHAPTER 2: LITERATURE REVIEW

Pregnancy

Stages of pregnancy

Pregnancy is the term used to describe the period of time it takes for a fetus to develop inside a uterus. Human pregnancy generally takes place over 40 weeks, or around 9 months, as measured from the last menstrual period until delivery of the baby. [10] Pregnancy is often referred to in three segments, called trimesters. The first trimester encompasses weeks 1-13, and begins after a sperm fertilizes an egg to form a zygote. [10,11] The zygote travels through the fallopian tubes, implants itself in the uterus, and forms a placenta, which connects the mother to the fetus and provides the fetus with nutrients and oxygen. [10] The first trimester marks the beginning of brain, spinal cord, heart, and other organ development. [10,11] Weeks 14-27 are referred to as the second trimester, and this often marks the baby's ability to move and hear. [10] The third trimester begins at week 28, is characterized by rapid fetal growth, and ends around 40 weeks when the baby is born. [10,11] Infants born preterm (before 37 weeks) are at increased risk for various problems such as cerebral palsy, vision and hearing problems, and developmental delays. [12] "Early term" infants born at 37 and 38 weeks are at less risk than preterm infants, but still face more health risks than those born "full term" at 39 and 40 weeks of pregnancy. [12]

Physiological changes

To accommodate for the growing fetus, the pregnant mother's body undergoes several anatomical, physiological, hormonal, and metabolic changes that affect every organ system in the body. [13] Haematological changes include a 50% increase in plasma volume with a concurrent fall in haemoglobin concentration, haematocrit, and red blood cell count, due to this haemodilution. [14] Pregnancy also produces a physiological hypercoagulable state, increasing fibrinogen levels by up

to 50% in anticipation of haemostasis following delivery. [15] Cardiovascular changes include increases in stroke volume, heart rate and a 40% increase in cardiac output, as well as increased ventricular wall muscle mass, myocardial contractility, and dilation. [16] Hormones produced by the corpus luteum, decidua, and placenta cause a 40% fall in systemic vascular resistance, which in turn causes renal vasodilation, increased renal plasma flow, and increased glomerular filtration rate. [17–19] These physiological changes lead to an increase in renal size of 1-1.5cm and dilation of the kidney and ureters. [19,20] Pregnancy also affects the respiratory system, causing a 40-50% increase in minute ventilation due to increased tidal volume early in pregnancy, and reduced functional residual capacity later in pregnancy. [16] Endocrine changes during pregnancy include an enlarged pituitary gland, altered production of thyroid hormones, and progressive increases in adrenal steroids. [16] Changes also occur within glucose metabolism to accommodate and provide for the fetus' requirement of glucose. [21]

Changes in insulin & glucose metabolism during pregnancy

The aforementioned physiological changes and maternal adaptations aim to ensure proper fetal development, while also maintaining maternal health. In the context of glucose metabolism, adaptations occur to shunt glucose to the fetus, promoting development, while also maintaining adequate maternal nutrition. [21] In early gestation, fasting blood glucose levels drop, remain steady throughout the second trimester, then further decrease during the third. [22,23] Additionally, increased fetal glucose utilization removes maternal glucose, and contributes to the decline. [22] During increased fetal glucose utilization, maternal insulin sensitivity decreases. To compensate for these changes and provide adequate maternal nutrition, maternal hepatic gluconeogenesis and fatty acid levels increase. [22] While fasting blood glucose levels remain lower than pre-pregnancy, postprandial (post meal) levels resolve to pre-pregnancy values. [24] This is thought to be the result

of impaired insulin action, and altered pancreatic B-cell-mediated insulin secretion and hepatic gluconeogenesis. [22]

In early pregnancy, there is a drop in growth hormone levels due to the presence of the fetus, resulting in enhanced insulin sensitivity (or, decreased insulin resistance). [25] Following this period, an increase in circulating levels of hormones such as human placental lactogen, growth hormone, progesterone, and prolactin interfere with insulin receptor signalling and cause a decrease in insulin sensitivity in adipocytes and skeletal muscle. [25] The effect of the placental hormones on insulin sensitivity is demonstrated by maternal insulin resistance that begins to increase in the second trimester and peaks in the third. [26] This insulin resistance reduces the amount of glucose uptake by maternal tissues, allowing more to be shunted to the fetus.

In response to the decline in maternal insulin sensitivity beginning in the second trimester, there is an adaptation to pancreatic β-cells, which synthesize and secrete insulin. Within the cell, an increase in the primary glucose sensor enhances glucose-stimulated insulin secretion at lower than normal blood glucose levels. [27] As well, prolactin and human placental lactogen mediate an increase in the size and number of β-cells, permitting an increase in insulin secretion. [27] This allows maternal uptake of glucose amid increased fetal glucose utilization, and promotes a reduction in blood glucose levels.

Opposingly, this increase in insulin secretion and concentration are contrasted by basal hepatic glucose production that can increase as much as 30% by late gestation. [28] During pregnancy, rates of hepatic gluconeogenesis progressively increase. [24] This raises maternal blood glucose levels and contributes to glucose homeostasis in order to maintain maternal euglycemia as fetal glucose utilization increases. [24]

Together, the decline in insulin sensitivity, adaptations to pancreatic β-cells, and increase in hepatic gluconeogenesis result in maternal insulin resistance, and balance the shunting of an adequate glucose supply to the fetus while maintaining maternal health. [21] Thus, pregnancy is characterized as a diabetogenic state. While the physiological adaptations occur naturally and usually manage to maintain maternal-fetal health, it is important to understand these changes such that should a pathological presentation of adaptations arise, it can be identified and treated.

Gestational Diabetes Mellitus

What is GDM?

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy. [8] GDM occurs when the normal pregnancy-related physiological insulin resistance becomes imbalanced, resulting in maternal blood glucose levels that rise to pathological values. [8] During a healthy pregnancy, insulin resistance increases with advancing gestation. [29] However, this effect is pronounced in women with GDM, who have markedly higher insulin resistance compared to their healthy counterparts. [29] In addition to decreased insulin sensitivity, women with GDM have reduced insulin secretion, as a result of a defect in β-cell adaptation.[22,29,30] Combined, the impairment in insulin secretion, higher levels of hepatic gluconeogenesis during pregnancy, and decrease in insulin sensitivity lead to elevated blood glucose levels and a diagnosis of GDM. [24]

In Canada, between 3% to 20% of pregnant women will develop GDM, depending on their risk factors.[1] Risk factors include: being 35 years of age or older, being from a high-risk ethnic group (African, Arab, Asian, Hispanic, Indigenous, South Asian), using corticosteroid medication, having obesity (Body Mass Index $\geq$30.0), prediabetes (blood sugar higher than normal, but not high enough to be considered type 2 diabetes), GDM in a previous pregnancy, having given birth

to a baby weighing more than 4kg, having an immediate family member with type 2 diabetes, and having polycystic ovary syndrome or acanthosis nigricans (darkened skin patches). [1] Diabetes Canada recommends that women who are at increased risk for GDM be screened earlier than the standard 24-28 weeks' gestation for early intervention in blood glucose management and reducing the associated risks of uncontrolled glycemia to mom and baby. [1]

GDM Clinical Care

Screening and diagnosis

Internationally, there is a lack of consensus on the criteria and method for the screening and diagnosis of GDM. [1] However, the method preferred by Diabetes Canada is a sequential two-step glucose test that tests pregnant women for impaired glucose tolerance (see Figure 1). [1] Due to the known progressive increase of insulin resistance from the second trimester into the third, Diabetes Canada recommends screening all pregnant women between 24 and 28 weeks' gestation, or earlier for women who have risk factors for overt diabetes or have previously had GDM. [1] In this two-step approach, a glucose challenge test (GCT) is administered first. This test is comprised of a 50g glucose beverage that is consumed non-fasted, and plasma glucose levels are tested 1 hour later. A 1 hour post-load plasma glucose (1hPG) value of <7.8 mmol/L is considered normal, whereas a value of ≥11.1 mmol/L results in a GDM diagnosis. Should the plasma glucose levels be between 7.8-11.0 mmol/L 1 hour after consumption of the beverage, patients are asked to come back for the second step. The second step is an oral glucose tolerance test (OGTT) that requires patients to consume a 75g glucose beverage after fasting for a minimum of 8 hours. The thresholds for GDM diagnosis based on a 75g OGTT are as follows: fasting plasma glucose (FPG) of ≥5.3 mmol/L, 1hPG of ≥10.6 mmol/L, and 2 hour later plasma glucose (2hPG) of ≥9.0 mmol/L. If any of these values is met or exceeded, GDM is diagnosed. Patients tested prior to 24 weeks' gestation

with a negative test result need to be reassessed between 24-28 weeks, due to the lack of validated thresholds for diagnosis of GDM prior to this time. [1]

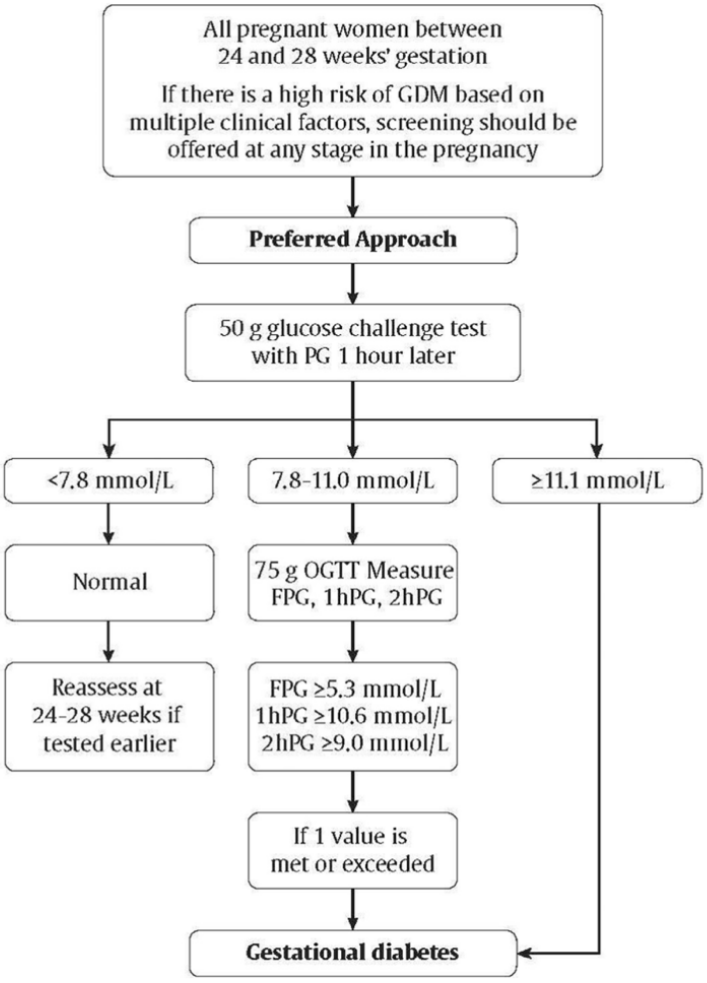


Figure 1. Diabetes Canada sequential two-step approach for the screening and diagnosis of gestational diabetes.
1hPG, 1-hour plasma glucose; *2hPG,* 2-hour plasma glucose; *FPG;* fasting plasma glucose; *OGTT,* oral glucose tolerance test.

Blood glucose monitoring

Throughout pregnancy, women with GDM must monitor their blood glucose levels to confirm that they have established glycemic control, and if not, to adjust accordingly. Diabetes Canada recommends frequent daily self-monitoring of blood glucose (SMBG), aiming for a FPG

and preprandial (pre-meal) glucose value of <5.3 mmol/L, a 1hPG of <7.8 mmol/L, and a 2hPG of <6.7 mmol/L. [1] While the optimal frequency of blood glucose testing has not been defined, it is recommended that glucose is monitored 4 times a day, once after fasting (upon wakening) and once after each meal (postprandially). [8] In women with GDM, blood glucose is commonly self-tested by using capillary blood from the fingertip on a testing strip and inserted into a glucometer. However, recent randomized controlled trials suggest that the use of a continuous glucose monitor (CGM) may be beneficial in the treatment of diabetes in pregnancy. A trial in which type 1 diabetic pregnant women (n= 215) either monitored their capillary blood glucose with or without a continuous glucose monitor (CGM) showed benefits to using a CGM. Participants who used a CGM spent more time in target glucose range and less time in hyperglycemia compared to pregnant controls. As well, the use of a CGM improved neonatal health outcomes, lowering the incidences of macrosomia (OR 0.51, 95% CI 0.28–0.90, p=0.021), neonatal intensive care unit admission longer than 24 hours (OR 0.48, 95% CI 0.26–0.86, p=0.0157), and incidences of neonatal hypoglycemia (OR 0.45; 95% CI 0.22–0.89, p=0.025). [31]

Another study randomized 340 participants with GDM into either routine care with SMBG or blinded 3-day CGM use every 2 to 4 weeks from GDM diagnosis. [32] Participants randomized to the CGM group compared to the routine care group were at lower risk of pre-eclampsia (3.4% vs. 10.1%, p=0.019) and primary caesarian delivery (34.7% vs. 46.6%, p = 0.028). Neonatal outcomes were more favourable in the CGM group compared to the routine care group, with lower risks for premature delivery (4.8% vs. 11.8%, p= 0.024), macrosomia (4.1% vs. 10.8%, p = 0.025), and hypoglycemia (5.5% vs. 14%, p = 0.011). While daily monitoring of blood glucose through a glucometer is associated with better outcomes than weekly office-based testing, CGM use may help identify hyper- or hypoglycemia that may be missed between daily tests. [33–35]

Monitoring maternal fasting glucose values may be important as they are associated with the development of childhood obesity and diabetes.[36] However, studies have demonstrated that managing both pre-pregnancy and gestational diabetes in pregnancy using the postprandial blood glucose measurement compared to preprandial was associated with reduced risk of macrosomia, lower rates of Caesarian sections, and better glycemic control. [5–7] As well, a 1 hour postprandial glucose value of <7.8 mmol/L is associated with better pregnancy outcomes. [6,37–40] Thus, Diabetes Canada and the ACOG recommend that management of blood glucose levels be based on postprandial as well as fasting values, and that a reasonable 1-hr postprandial blood glucose target value is <7.8 mmol/L. [1,8]

Postprandial glucose profile

The characteristics of the postprandial glucose profile differ between pregnancies that are affected by diabetes and those that are not. [41] In the typical pregnant postprandial glycemic profile, glucose levels rise following a meal, 1hPG and 2hPG averaging at 6.04 ± 0.72 mmol/L (108.9 ± 12.9 mg/dl) and 5.5 ± 0.57 mmol/L (99.3 ± 10.2 mg/dl) respectively, and then fall back to preprandial levels. [41] Hernandez et al. (2011) found that average time to peak postprandial blood glucose was 69.4 ± 23.9 minutes. [41] However, the average time to peak glucose levels in pregnancies affected by diabetes is longer, at approximately 90 minutes following a meal, and the peak is higher than in normal pregnancies. [42,43] Furthermore, Ben-Haroush et al. (2004) demonstrated that in a mixed group of pregnant GDM and type 1 diabetes patients, approximately 50% failed to return to preprandial glucose values within 3 hours after a meal. [42] It is evident that the glycemic profile of pregnant individuals with diabetes differs from that of a normal pregnancy, and knowing that postprandial blood glucose values are associated with better pregnancy outcomes, it is important to focus on glucose management at this timepoint.

Hypoglycemia

Traditionally, hypoglycemia is defined as a blood glucose <4.0 mmol/L. However, as pregnancy lowers blood glucose levels by 20%, the American Diabetes Association and Endocrine Society Working Group define hypoglycemia during pregnancy as a blood glucose <3.3 mmol/L. [44,45] It is difficult to establish an official lower limit of blood glucose during pregnancy as hypoglycemia can differ between people with diabetes, depending on symptoms, therapy, associated risk, and medical condition. [1] Hypoglycemia that is not sustained, and is not associated with trauma, convulsion, or loss of consciousness, is considered to be without risk for the fetus. [46–48] However, due to the maternal risks of hypoglycemia, Diabetes Canada recommends that pregnant women with diabetes who have been prescribed insulin therapy should have a glucagon kit, be aware of effective interventions to reverse a severe hypoglycemic event, inform family and co-workers of the risk of hypoglycemia, and maintain blood glucose values of >3.7 mmol/L. [1]

Management: Dietary

Currently, GDM front-line therapies include dietary modifications, exercise, and pharmacological treatments.[8] While the actual dietary composition that optimizes perinatal outcomes is unknown, there have been several randomized trials with various dietary modifications that demonstrated success in improving pregnancy outcomes. These include low-glycemic index nutrition plans, high-fiber diets, and complex carbohydrate diets.[49,50] Diabetes Canada recommends that women follow a low-glycemic index diet, replacing high-glycemic index foods with low-glycemic index foods, but consume a minimum of 175g/day of carbohydrates distributed over three meals and two snacks. [1,8,51] However, current evidence for this type of diet is limited, and thus meal planning for women with GDM should emphasize an overall healthy diet.

[1] While dietary interventions help control blood glucose levels, they are often prescribed along with a recommendation for physical activity.

Management: Physical activity and exercise

In addition to nutritional intervention, and prior to pharmacological therapies, Diabetes Canada encourages women with GDM to partake in physical activity. [1] Barring contraindications to exercise (see Table 1), it is recommended that in order to achieve clinical meaningful reductions in pregnancy complications, all pregnant women should aim to aerobically exercise for 30 minutes a day, 5 times a week, or 150 minutes per week, at a moderate intensity.[8,9] Absolute contraindications provide indication for cessation of activities beyond usual activities of daily living. [9] However, women with relative contraindications to exercise should consult their health care provider to discuss exercise modifications and suggested intensities of physical activity. [9] In addition to showing improvements in gestational weight gain and blood glucose, the recommended exercise prescription was associated with clinically meaningful reductions in the odds of developing GDM, pre-eclampsia, and gestational hypertension. [9] The 2019 Canadian Guideline for Physical Activity throughout Pregnancy especially recommends physical activity during pregnancy for obese or overweight women, based on evidence from randomized controlled trials showing improvements in gestational weight gain and blood glucose. [52–54]

Table 1. Absolute and relative contraindications to physical activity during pregnancy.

Absolute contraindications	Relative contraindications
♦ Ruptured membranes, premature labour.	♦ Recurrent pregnancy loss.
♦ Unexplained persistent vaginal bleeding.	♦ History of spontaneous preterm birth.
♦ Placenta praevia after 28 weeks' gestation.	♦ Gestational hypertension.
♦ Pre-eclampsia.	♦ Symptomatic anaemia.
♦ Incompetent cervix.	♦ Malnutrition.
♦ Intrauterine growth restriction.	♦ Eating disorder.
♦ High-order multiple pregnancy (eg. triplets).	♦ Twin pregnancy after the 28th week.
♦ Uncontrolled type I diabetes, uncontrolled hypertension or uncontrolled thyroid disease.	♦ Mild/moderate cardiovascular or respiratory disease.
♦ Other serious cardiovascular, respiratory or systemic disorder.	♦ Other significant medical conditions.

Note: Reprinted from *2019 Canadian guideline for physical activity throughout pregnancy* by Mottola et al. (2018).

Management: Medications

Diabetes Canada recommends that if women with GDM do not achieve their blood glucose targets within 2 weeks of the implementation of nutritional and exercise intervention, pharmacological treatments should be initiated. [1] The two most common pharmacological treatments are the use of exogenous insulin and metformin. Insulin is most effective in reducing fetal and maternal morbidity when using multiple daily injections in order to continuously adjust glycemia throughout the day. [55–57] Rapid-acting insulin (mimicking endogenous insulin and peaking about 1 to 2 hours after injection), such as aspart and lispro, help achieve postprandial blood glucose targets with less hypoglycemia than regular insulin (peak at 2 to 3 hours after injection), and with similar fetal outcomes. [58] Long-acting insulin also appears to be effective, and can be used to treat fasting hyperglycemia. [58] While insulin does not cross the placenta and is considered a safe pharmacological treatment, individuals can be at risk for hypoglycemia.

An alternative and more convenient pharmacological therapy is the use of Metformin, an oral antidiabetic drug that improves insulin sensitivity and supresses hepatic glucose production. [59] The use of Metformin compared to insulin has been associated with less weight gain and less pregnancy-induced hypertension, and for these reasons may be a good choice. [60,61] However, Metformin does cross the placental barrier. [62] While Metformin exposure does not seem to be harmful on fetal outcomes, longer-term follow up on motor, linguistic, social, metabolic, and neurological developments throughout adulthood are not yet available. [1,62–65]

In summary, insulin or Metformin can be used to treat patients with GDM, and the treatment of choice should be tailored for each patient, depending on their glycemic profile and preferences. [58] While pharmacological treatments are deemed safe, effective, and part of conventional GDM care, the associated risks lead experts to recommend dietary and exercise intervention as front-line therapies, followed by medication if needed.[8]

Health implications of GDM

Short-term complications and consequences for maternal and neonatal health

The key target in treating GDM is normalizing blood glucose values. [1] Previous studies have demonstrated that poorly controlled fasted and postprandial blood glucose contributes to an increased risk of pregnancy complications and adverse outcomes for both the mother (e.g. pre-eclampsia, caesarian delivery) and baby (e.g. birth weight >90th percentile, neonatal hypoglycemia). [2–4,37,66] This includes an elevated risk of pre-eclampsia, a maternal pregnancy complication that presents itself as high blood pressure and damage to other organ systems. [66] Uncontrolled maternal blood glucose values in GDM poses a 32% increased risk in gestational hypertension (high blood pressure). [67]

In a group of individuals with mild, but uncontrolled gestational diabetes (n = 473), the frequency of large-for-gestational-age infants was more than double that of the treatment group (n = 485) (14.5% vs. 7.1%). [37] The rate of shoulder dystocia, a birth complication in which the baby's shoulder gets caught on the maternal pubic bone, causing potential birth injury, was also more than double in the untreated group (4.0% vs. 1.5%). [37] As for maternal outcomes, rates of pre-eclampsia and gestational hypertension were higher in the untreated group than the treatment group (combined rates, 13.6% vs. 8.6%, p = 0.01). [37]

A large, multicenter, international prospective cohort (n = 23,316) study examined the association of maternal glycemia with increased risk of adverse pregnancy outcomes. [66] The researchers calculated adjusted odds ratios (OR) of adverse pregnancy outcomes (primary caesarian delivery, premature delivery, neonatal hypoglycemia, birth injury, birth weight >90th percentile and preeclampsia) associated with a 1 SD (standard deviation) (0.4 mmol/L) increase in fasting plasma glucose levels, a 1 SD (1.7 mmol/L) increase in the 1-hour after an oral glucose tolerance test (OGTT), and a 1 SD (1.3 mmol/L) increase in the 2-hours after an OGTT. All three measurements of glucose control were positively associated with an increase in the odds of adverse birth outcomes (Table 2). Although this study did not have the statistical power to investigate perinatal death as a primary outcome related to blood glucose measurements, unadjusted OR of 0.91 (0.76 to 1.08), 0.93 (0.78 to 1.11), and 0.99 (0.83 to 1.18) did not show an increase in the odds of perinatal death.

Table 2. Adjusted odds ratios (OR) for associations between maternal glycemia and adverse pregnancy and birth outcomes.

Outcome	Plasma Glucose Level		
	Fasting	1 hr post OGTT	2 hrs post OGTT
	Odds ratio (95% CI)		
Primary caesarian delivery	1.11 (1.06-1.15)	1.10 (1.06-1.15)	1.08 (1.03-1.12)
Premature delivery	1.05 (0.99-1.11)	1.18 (1.12-1.25)	1.16 (1.10-1.23)
Neonatal hypoglycemia	1.08 (0.98-1.19)	1.13 (1.03-1.26)	1.10 (1.00-1.12)
Birth injury	1.18 (1.04-1.33)	1.23 (1.09-1.38)	1.22 (1.09-1.37)
Birth weight >90th percentile	1.38 (1.32-1.44)	1.46 (1.39-1.53)	1.38 (1.32-1.44)
Pre-eclampsia	1.21 (1.13-1.29)	1.28 (1.20-1.37)	1.28 (1.20-1.37)

Data presented as adjusted odds ratio (95% CI) of adverse pregnancy outcomes associated with a 1 SD (0.4 mmol/L) increase in fasting plasma glucose levels, a 1 SD (1.7 mmol/L) increase in the 1-hour after an OGTT, and a 1 SD (1.3 mmol/L) increase in the 2-hours after an OGTT.

A study in France also investigated the risk of adverse perinatal outcomes in GDM in a large national cohort (n = 716,152). [68] Compared to pregnancies uncomplicated by GDM, those with GDM had increased risks of adverse outcomes. For caesarian delivery, the OR was 1.4 (95% CI, 1.4 to 1.4); for premature delivery, 1.3 (1.3 to 1.4); for birth trauma, 1.3 (1.1 to 1.5); for cardiac malformations, 1.3 (1.1 to 1.4); for macrosomia, 1.8 (1.7 to 1.8); and for pre-eclampsia, 1.7 (1.6 to 1.7). This study observed a higher risk of perinatal mortality for those with GDM, with an OR of 1.3 (95% CI, 1.0 to 1.6). Other studies have also found glucose measurements to be associated with increased odds of an infant's birth weight above the 90th percentile, which is associated with dangers during delivery such as fetal asphyxia, and future health risks such as offspring obesity. [69–72] However, the normalization of maternal blood glucose values can significantly decrease the risks of adverse outcomes, such as macrosomia by 53%, birth injury by 58%, and gestational hypertension by 32%. [67] Thus, it is critically important to manage maternal blood glucose levels in GDM, for the health of both mother and baby.

Long-term consequences for maternal and offspring health

While higher levels of blood glucose are associated with delivery complications along with short-term health risks for the mother and baby, they are also associated with longer-term adverse outcomes. High circulating maternal blood glucose may persist past gestation; although hyperglycemia usually resolves following delivery, women with a history of GDM are at risk for postpartum impairment of insulin secretion and action and future type 2 diabetes. [73,74] Between 3 to 6 months postpartum, there is a 16-20% risk of dysglycemia (abnormal blood sugar regulation) for women with a history of GDM. [1] Within the first 3 years after giving birth, individuals with a history of GDM are 8 times more likely to develop type 2 diabetes. [75] As well, compared to normoglycemic individuals, those with a history of GDM are 7.43 times more likely to develop type 2 diabetes after giving birth. [76] Sixteen years following a GDM diagnosis, 40% of women develop type 2 diabetes. [77] The finding that a history of GDM is associated with an increase in the development of type 2 diabetes is reasonable, given that along with common risk factors such as family history, BMI, and prediabetes, women with GDM often present with a defect in β-cell function (where insulin secretion does not rise adequately in response to increased insulin resistance), and this defect is also present in those who develop type 2 diabetes. [78,79]

The development of GDM also carries potential long term maternal cardiovascular health consequences. [76,80] One study reported that when compared to their healthy counterparts, women with a history of GDM were at higher risks of obesity, hypertension, and dyslipidemia, with respective risk ratios of 2.4, 7.5 and 2.4. [81] Another study reported a hazard ratio for cardiovascular disease events following a history of GDM to be 1.71. [82]

Not only are there long-term health risks for the mother, but impaired maternal glucose tolerance also poses risks for offspring of women with a history of diabetes during pregnancy. [83,84]

Adult offspring of women with diet-treated GDM were twice as likely to be overweight compared to an unexposed reference group, and has a 4-fold increased risk of metabolic syndrome (cluster of conditions including obesity, abnormal cholesterol levels, abnormal triglyceride levels, high blood pressure, and/or high blood sugar). [84] This risk increased in tandem with increasing maternal fasting blood glucose levels and 2hPG following an OGTT. [84] Not only does GDM increase the risk of maternal development of type 2 diabetes, but a hyperglycemic uterine environment (in addition to genetics), as is the case in GDM, also predisposes offspring to an increased risk of adulthood type 2 diabetes or pre-diabetes. [83] The OR for offspring of women with GDM was 7.76 (95% CI, 2.58 to 23.39), compared to offspring from a background population.

The health risks posed to both mother and baby associated with GDM are amplified when blood glucose levels are poorly controlled. [1] Thus, GDM is an important period of time in which interventions need to be made in order to reduce the risk of cardiovascular disease, progression to type 2 diabetes, and adverse neonatal outcomes. [85]

Exercise for the management of GDM

Chronic metabolic response to exercise in GDM

Though published trials have small sample sizes, regular exercise may help maintain fasting and postprandial normoglycemia, in addition to enhancing maternal insulin sensitivity and reducing the need for insulin use. A 2013 review reported that five out of seven (71%) prenatal physical activity interventions were successful in improving glycaemic control and/or limiting insulin use in women with GDM. [86] In all studies, women in both the control and intervention groups received the minimum standard GDM care of nutrition therapy intervention. A more recent review evaluated the effects of randomised controlled trial (RCT) exercise interventions on outcomes in women with GDM. [87] This review found exercise interventions to be associated with

reduced fasting blood glucose levels (average standardised mean difference (SMD) -0.59, 95% CI -1.07 to -0.11; 4 RCTs, 363 women) and reduced postprandial blood glucose concentration (average SMD -0.85, 95% CI -1.15 to -0.55; 3 RCTs, 344 women), compared with control interventions.

A 6-week, aerobic, arm ergometry exercise RCT successfully normalized FPG and 1hPG in women with GDM whose intervention consisted of nutrition therapy plus exercise, compared to nutrition therapy alone. [88] Women exercised three times a week for 20 minutes at an intensity ≤ 50% VO_2max. At the end of the intervention period, the exercise group had significantly lower FPG than the control group (3.89 ± 0.37 mmol/L (70.1 ± 6.6 mg/dl) vs. 4.86 ± 0.34 mmol/L (87.6 ± 6.2 mg/dl), $p < 0.001$). The mean 1hPG after an OGTT in the exercise group (5.88 ± 1.05 mmol/L (105.9 ± 18.9 mg/dl) was also significantly lower ($p < 0.001$) than the control group (10.41 ± 0.72 mmol/L (187.5 ± 12.9 mg/dl). None of the women in the study required insulin. Another RCT utilizing aerobic exercise randomized participants to a nutrition plus insulin group or a nutrition plus exercise group. [89] Participants entered the study at an average of 30 weeks' gestation. Women in the exercise group exercised aerobically three times per week for 45 minutes on a stationary cycle ergometer at 50% VO_2max. No difference in mean blood glucose was found between intervention groups, suggesting that exercise may increase insulin sensitivity, reducing the need for exogenous insulin. Bo et al. (2014) conducted an RCT to test whether four different lifestyle programs could improve blood glucose control in women with GDM. [90] The four groups consisted of: diet only, diet plus behavioural recommendations, diet plus aerobic exercise, and diet plus behavioural recommendations plus aerobic exercise. The groups prescribed exercise were advised to walk for a minimum of 20 minutes per day at a perceived moderate intensity (Borg scale 12-14), totaling 140 minutes per week. While fasting glucose levels did not change between groups

post-intervention, exercise, but not behavioural recommendations, was associated with a decrease in postprandial glucose ($p < 0.001$). Exercise groups had a mean postprandial glucose value of 5.89 ± 1.05 mmol/L (106.1 ± 19.0 mg/dl), whereas non-exercise groups had a mean of 6.5 ± 0.92 mmol/L (117.2 ± 16.5 mg/dl). There was no significant difference between groups' requirement of insulin.

Another RCT had varying results, with improvements in postprandial blood glucose but not in the response to an OGTT. Halse et al. (2014) reported that participants with GDM randomized to an exercise plus conventional management versus conventional management only managed to reduce their capillary glucose concentrations in response to each exercise session (6.3 ± 0.8 mmol/L to 4.9 ± 0.7 mmol/L, $P < 0.001$). [91] The exercise group also had a lower postprandial glucose concentration mean compared to their counterparts ($p = 0.046$). Participants in the exercise group completed 1 session per week of supervised stationary cycle ergometry that progressed from 25- to 30-minute sessions at 55-65% age-predicted HRmax to 45 minutes over the 6-week intervention period. Participants were also instructed to perform 30 minutes of unsupervised moderate-intensity aerobic activity of their choice on two other days of each week. There was high compliance to the supervised cycling sessions (96%) and the unsupervised sessions (2 ± 1 sessions/week), with 52% of participants completing walking sessions, 40% stationary cycling, 5% engaging in aquatic exercise, and 3% partaking in yoga. While the intervention did not improve glucose tolerance or the insulin response to an OGTT, the postprandial blood glucose improvement may be beneficial for mom and baby, given the health implications resulting from maternal hyperglycemia.

Brankston et al. 2004 randomized women with GDM into nutrition intervention only and nutrition plus circuit-type resistance training. [92] While the number of women requiring insulin did

not differ between the groups, within the nutrition plus exercise group, 30% of women who exercised 2-3 times per week were prescribed insulin, compared to 67% of women who exercised less than twice per week. Also using resistance (elastic band) training versus nutrition therapy, de Barros et al. 2010 conducted an RCT that showed an association between exercise and a reduction in the number of women who needed insulin. [93] Additionally, the exercise group spent more time in the target glucose range than the nutrition group. Compliance in this intervention was very good, with an average of 2.36 ± 0.4 exercise sessions per week that lasted 30-40 minutes.

Another study compared 10 women following standard GDM care plus a low intensity walking program (30% heart rate reserve, average of 3.6 ± 0.8 exercise sessions per week) to 20 women matched by insulin use who followed standard GDM care alone. [94] Findings from this study reported lower fasting and postprandial blood glucose levels at the end of pregnancy compared to the beginning of the intervention in the walking group ($p < 0.05$), and lower glucose levels compared to the control group ($p < 0.05$). Additionally, women in the walking group required fewer units of insulin per kilogram per day compared to the control group (0.16 ± 0.13 $U \cdot kg^{-1}$ vs. 0.50 ± 0.37 $U \cdot kg^{-1}$, $p < 0.05$).

While several interventions were successful, two were not with respect to improving glycaemic control or decreasing the need or amount of insulin use. A partial home-based RCT exercise program (three to four 30 minute sessions at 70% estimated maximal heart rate from about 27 weeks' gestation to the end of pregnancy) did not show a difference in glucose excursion when compared to women without a structured exercise program. [95] There was no significant difference in requirement of insulin therapy between groups post-intervention ($p = 0.65$). In another study, women with obesity and GDM were divided into nutrition therapy or nutrition therapy plus

exercise (daily exercise sessions of 20 minutes at 60% VO_2max). [96] Adherence was low, with only 50% of the women meeting the recommendation of >150 minutes/week of exercise.

Although not all interventions were successful, many interventions had successes that improved outcomes relevant and important to GDM and its management. Reductions in fasting and postprandial blood glucose, as well as a decrease in the amount of insulin required indicate that regular prenatal exercise may be an important element in the treatment and management of GDM.

Acute metabolic response to exercise in GDM

Research concerning the implementation of exercise to manage GDM has largely focused on chronic interventions, their effects on blood glucose levels and insulin response. Although international bodies recommend short walks after meals to help control blood glucose, few studies have investigated the acute effects of exercise and exercise timing on postprandial blood glucose response. [8] To date, three studies have examined the acute effects of exercise on glucose metabolism in women with GDM. [97–99]

Lesser et al. (1996) reported that a single bout of exercise did not blunt the postprandial glycemic response. [97] In this study, five women without GDM and six women with GDM completed a 30 minute stationary cycling session at 60% VO_2max, 14 hours prior to a meal, to simulate the effects that an evening workout could have on metabolism the following day. They returned to the laboratory the next morning in a fasted state and were fed a mixed-nutrient breakfast. Their blood glucose was measured at fasted state, and at 1, 10, 30 minutes and then 30 minute intervals up to 180 mins postprandially. Participants also completed an alternate protocol either 1 week before or 1 week after, in which they consumed the same meal, but did not partake in an exercise session the evening prior. Results from this study indicated that an acute bout of

exercise done 14h prior to consuming a mixed-nutrient did not blunt the glycemic response. Between protocols, there were no significant differences observed in fasting glucose and insulin levels, peak glucose and insulin levels, and area under the curve of glucose ($p = 0.31$) and insulin ($p = 0.43$), in either participant group. Thus, the researchers concluded that improved glycemic control may be due to the chronicity of training rather than individual events. However, the exercise session completed by their participants was many hours prior to the meal, and the effects of exercise may have been diminished by the time the meal was served.

Avery and Walker (2001) aimed to examine the acute effects of exercise on blood glucose and insulin levels at two exercise intensities, 35% VO_2max (low intensity) and 55% VO_2max (moderate intensity), compared to rest, in women with GDM.[98] Thirteen women visited the laboratory on 3 separate occasions, 90 minutes following a mixed-nutrient meal. Participants then either rested in a for 30 minutes, or exercised at one of the two intensities for 30 minutes on a cycle ergometer. Blood samples were taken at 15-minute intervals throughout the exercise and rest, and for 2 hours following the conditions. Results from the study demonstrated that at the end of exercise, mean blood glucose levels were significantly lower compared to resting (5.2 ± 0.77 mmol/l), and were lower for the moderate-intensity than the low-intensity (3.9 ± 0.52 mmol/l vs. 4.3 ± 0.52 mmol/l). At 15 minutes following exercise, mean blood glucose levels were still significantly lower in the exercise conditions compared to rest (4.9 ± 0.81 mmol/l), but not significantly different from each other (4.0 ± 0.38 mmol/l vs. 4.4 ± 0.54 mmol/l). This effect did not persist past 15 minutes of exercise; at 30 minutes after exercise, mean blood glucose levels did not significantly differ, and at 45 minutes were all nearly identical. Results from this study indicate that a 30 minute bout of low or moderate intensity exercise is effective at temporarily reducing

blood glucose concentration, however its potential effect on postprandial blood glucose levels still remains to be investigated.

In an attempt to investigate the effects of a light intensity exercise session on postprandial blood glucose in women with GDM, Garcia-Patterson et al. (2001) recruited 20 women with GDM to walk self-paced for an hour after a standard breakfast, and remain seated for the second hour. [99] The women also completed a control day, in which their blood glucose was measured at fasting, 1 hour, and 2 hours after their meal. Significant differences were observed in their 1 hr postprandial exercise blood glucose compared to their control day (5.35 ± 0.69 mmol/l vs 6.02 ± 0.78 mmol/l), although no differences were observed in their fasting and 2 hour postprandial blood glucose. This research indicated that 1 hour of continuous light postprandial exercise was effective in blunting the glycemic response after breakfast, a meal, but no longer than 1 hour postprandially. While successful, this method of reducing postprandial blood glucose is in reality not a practical method for women to reduce their blood glucose following each meal. Depending on lifestyle, a 1-hour walk after each meal may not be feasible due to time constraints and potentially anthropometric constraints, which would most likely lower adherence. Additionally, a potential difference in blood glucose response to exercise depending on the time of day should be considered; blood glucose values vary throughout the day, and are on average higher during the day than during sleep. [100,101] Perhaps shorter, but more frequent bouts of exercise would increase feasibility, ensure adherence, and help determine the influence of exercise on blood glucose at various timepoints throughout the day.

In summary, previous studies have shown that acute bouts of exercise are successful in reducing blood glucose levels, and if completed in a timely manner following a meal, can help

reduce 1 hour postprandial values. However, the practical application of exercise duration and feasibility of the type of exercise must be taken into consideration.

Barriers to exercise

Important considerations when prescribing exercise are barriers to physical activity and compliance to prescribed programs. Despite the benefits of exercise, many women with GDM remain sedentary. [102] Women with GDM cite a lack of time, lack of access to equipment, taking care of children, and fatigue as barriers to exercise. [102] Pregnancy can induce stress and anxiety for women, and a diagnosis of GDM can increase the emotional and physical stress they feel. [102] Thus, it is recommended that healthcare providers take into account patients' feelings towards exercise and their perceived barriers to exercise when prescribing exercise programs to manage blood glucose levels.

Summary

Findings from chronic exercise interventions in women with GDM demonstrating improved blood glucose regulation suggests that exercise may be an important element in the treatment and management of GDM. It is recommended that in addition to fasting levels, the management of blood glucose in GDM be based on postprandial levels due to the associated reduction in risk of adverse pregnancy outcomes. However, while acute exercise sessions have been shown to have temporary effects on reducing blood glucose levels, the optimal timing of exercise bouts around meals has yet to be determined. Diabetes Canada and the American College of Obstetricians and Gynecologists recommend that pregnant women diagnosed with GDM aim to complete 150 minutes of aerobic exercise per week, suggesting that multiple 10 minutes bouts could be as effective as a single longer session. [8] The ACOG recommends pregnant women with GDM take 10-15 minute walks after eating, however this recommendation was based on expert

opinion and not empirical evidence.[8] Recent evidence demonstrated that short 15-minute bouts of exercise reduced blood glucose levels during pregnancy by an average of 0.5 mmol/L. [103] However, the glycemic outcomes of multiple short bouts of exercise totaling 30 minutes daily have not been compared to daily bouts of 30 minutes of exercise. As well, the effects of multiple short bouts of daily exercise have not been evaluated postprandially. Thus, I propose to compare the effects of shorter, postprandial bouts of exercise to longer, fasted bouts of exercise on blood glucose regulation.

CHAPTER 3: METHODS

Ethical Approval

Approval for this study was received by the Health Research Ethics Board – Biomedical Panel of the University of Alberta (Pro00097525). Written informed consent will be obtained from all participants prior to participation.

Participants

Participants were residents of Canada who had singleton pregnancies and either had a diagnosis of GDM or an uncomplicated pregnancy. Those with GDM had otherwise uncomplicated pregnancies. Due to COVID-19, 6 participants with gestational diabetes (GDM) and 6 participants without (NON-GDM) volunteered to participate, and written informed consent was obtained from each participant. Two participants (1 GDM, 1 NON-GDM) dropped out prior to study participation due to medical reasons unrelated to the study. As GDM is generally screened for and diagnosed toward the end of the second trimester, participants were recruited after 20 weeks' gestation. Women were excluded if they had absolute contraindications to prenatal exercise (Table 1) as identified by the PARmed-X for Pregnancy[104] or the 2019 Canadian Guideline for Physical Activity Throughout Pregnancy[9].

Participant recruitment occurred nationally and through various methods. Posters and a pre-recorded video presentation were created and distributed to Diabetes and Pregnancy clinics, obstetric clinics, the Edmonton Zone Diabetes Program Quality Council, and GDM education classes provided through Alberta Health Services and Covenant Heath. Participants were also recruited through the research website (www.per.ualberta.ca/exerciseandpregnancy) and social media (Facebook and Instagram).

Experimental Design

This was a randomized cross-over study design comparing two different exercise prescriptions for pregnant women with and without GDM. Participants were randomized to start with one of two study conditions using a randomization scheme (www.sealedenvelope.com), and then completed the complementary condition. The randomization was completed by a researcher external to the investigative team, and assignments were sequentially provided as each participant consented.

Study Period

Potential volunteers were provided with an information sheet detailing the research project and were invited to speak with a researcher about the study. In this initial consultation, the components of the study were fully explained and questions were answered. If the individual volunteered to participate in the study, voluntary written informed consent was obtained. Volunteers were reminded of their right to withdraw from the study at any time, for any reason. A Health History Questionnaire was completed prior to participation in the exercise portion of the study to confirm eligibility.

The study period began with two days of normal daily physical activity (NORMAL), followed by five consecutive days of the first intervention condition, then a washout period of two days of normal daily physical activity, followed by five days of the second intervention condition (see Figure 2). Participants were randomized into their first intervention condition of either three 10-minute postprandial walks (SHORT), or one 30-minute bout of walking (LONG) per day. Following written consent, participants were provided with a package containing their intervention assignment, instructions, and all the materials required for participation. Participants met one-on-

one over secure video chat (doxy.me) with the researcher to become familiar with the equipment and protocol. At the end of the study period, all materials were returned to the laboratory by mail.

Exercise Protocol

Participants completed two days of baseline blood glucose and activity monitoring beginning the morning after their initial meeting. Women randomized to the SHORT condition first were asked to complete 10-minute walks within in the first hour after breakfast, lunch and dinner for five days. Those randomized to the LONG condition were to complete 30 minutes of walking at any time of day other than the hour immediately following breakfast, lunch or dinner for five days. Walking was the prescribed modality because of its accessibility, feasibility and low cost. [105] In both exercise conditions, participants were asked to walk at a self-selected light-to-moderate physical activity intensity and wear a heart rate monitor (Polar) in order to confirm they were in the prescribed intensity range (light; 101-124 bpm, moderate; 121-146 bpm) [9]. Both exercise intervention conditions met the current physical activity recommendations for pregnant women of 150 minutes/week of moderate-intensity aerobic exercise. [9] Following the two-day washout period, participants were asked to complete the complementary exercise protocol for five days. Throughout the study, participants wore a flash glucose monitor to measure interstitial fluid glucose and an accelerometer to measure physical activity.

Instrumentation

Flash Glucose Monitor

Participants were provided with the FreeStyle Libre Pro Flash Glucose Monitoring System (Abbott, Chicago, IL, USA) to wear for the entirety of the study period. This professional flash glucose monitoring device (FGM) is the size of a loonie and adheres to the skin. This minimally invasive monitor detects and records interstitial fluid glucose levels at 5-minute intervals for up to

two weeks. This data is recorded internally and can be viewed on the handheld reader after scanning over the sensor. The data is presented as a graph displaying glucose levels over any given day. The FGM was applied after designating a site on the back of the upper arm and cleaning it with an alcohol wipe. The device comes with an applicator containing a needle, which is joined with the sensor to facilitate application. Once the arm was dry, the sensor applicator was placed over the site and a firm push guided the needle and filament under the skin. The needle was automatically and immediately removed. One hour after application, participants followed written instructions to activate the sensor on a handheld reader. Participants were able to scan their FGM and view their glucose graph throughout the duration of the study. At the end of the study period, participants returned the sensor and reader, and data was downloaded using the Freestyle Libre Pro software for desktop (Abbott, Chicago, IL, USA). Participants with GDM were asked to follow their healthcare provider's guidance for GDM management, including continuing their capillary blood glucose measurements, diet recommendations and medications as prescribed.

The use of the Freestyle Libre Flash Glucose Monitoring System has previously been evaluated in pregnant women with type 1, type 2, and gestational diabetes. [106] The Freestyle Libre System Sensor glucose values demonstrated good agreement with SMBG glucose values (capillary blood glucose measures made at least 4 times per day). [106] Importantly, the accuracy of the sensor remains stable at all times, including throughout rapidly changing glucose values, such as in the postprandial state. [106] As well, accuracy was unaffected by insulin use, stage of pregnancy, BMI (body mass index), or age. [106] The study reported several adverse pregnancy events, but none related to the study device or procedure. [106] While 5 out of 74 participants reported signs or symptoms related to sensor application (bleeding, bruising, itching, pain, and redness of the skin), they were all mild and resolved upon study completion (between 12 to 15 days). Thus, the accuracy

and safety of the Freestyle Libre System for use in pregnant women with diabetes has been demonstrated.

Accelerometer

Participants were asked to wear an accelerometer (Actigraph wGT3X-BT Monitor, Actigraph LLC, Pensacola, FL, USA) for the entire study period (14 consecutive days and nights) to record 24-hour physical activity measurements. This information was collected to determine overall physical activity and movement behaviours (including activity intensity). An accelerometer is a small device that is roughly the size of a matchbox and attaches to a waist or wrist strap. Participants wore the accelerometer on their waist during the day and on a wrist strap at night. The accelerometer monitors activity but does not provide any feedback/data to the wearer or the researcher during the 14-day wear period. Participants were asked to fill in a log during this time indicating when the device was being worn, and when they doing activities. Accelerometers were returned to the laboratory at the end of the study period and activity data was downloaded by the researcher onto specific software (ActiLife 6, Actigraph LLC) and analysed for activity levels.

The ActiGraph wGT3X-BT records continuous physical activity information using publicly available algorithms. Measures that were recorded include: Raw acceleration (G's), activity counts, active energy expenditure (kcals), METs, steps taken, physical activity intensity, activity bouts, and sedentary bouts. The wGT3X-BT provides valid estimates of moderate- and vigorous-intensity physical activity in adult populations. [107] The device has also been shown to be less affected by walking style and have less variability in pregnant women when worn on the waist, providing an indication for waist-wearing during times of physical activity. [108] This accelerometer has been used in previous studies of pregnancy to measure physical activity. [109]

Heart Rate Monitor

Participants were lent a heart rate monitor chest strap (Polar, Kempele, Finland) to wear during their walking sessions to confirm they were in the prescribed intensity range (101-146 bpm). The chest strap is worn around the chest with the sensor placed just inferior to the sternum. It wirelessly connects to the Polar Beat mobile application (downloaded through the Apple App Store or Google Play), which displays heart rate in beats per minute (bpm). This device was returned to the researchers at the end of the study period.

Food Intake Record

In order to determine caloric and nutritional intake as well as time of meals, participants were asked to keep a log of their food consumption for the entire study period (14 days). Participants recorded when they ate their meals and the specifics of the foods they consumed such as type, brand, amount, condiments, and any ingredients used for cooking (e.g. butter, oil). They were instructed to be as detailed as possible, describing individual ingredients for all of their food intake. Participants were also provided with a guide to determine the amount (volume) of food items or ingredients they consumed, rather than weighing them. Food intake records were returned to the laboratory at the end of the study period, and information regarding diet intake was derived from these records.

Questionnaires

Participants were asked to complete a Health History Questionnaire (HHQ) in order to screen for any current absolute contraindications to exercise during pregnancy that might be considered unsafe or render a participant ineligible for the study. The HHQ also served to obtain participant demographic, anthropometric, and health information such as weight, height, ethnicity,

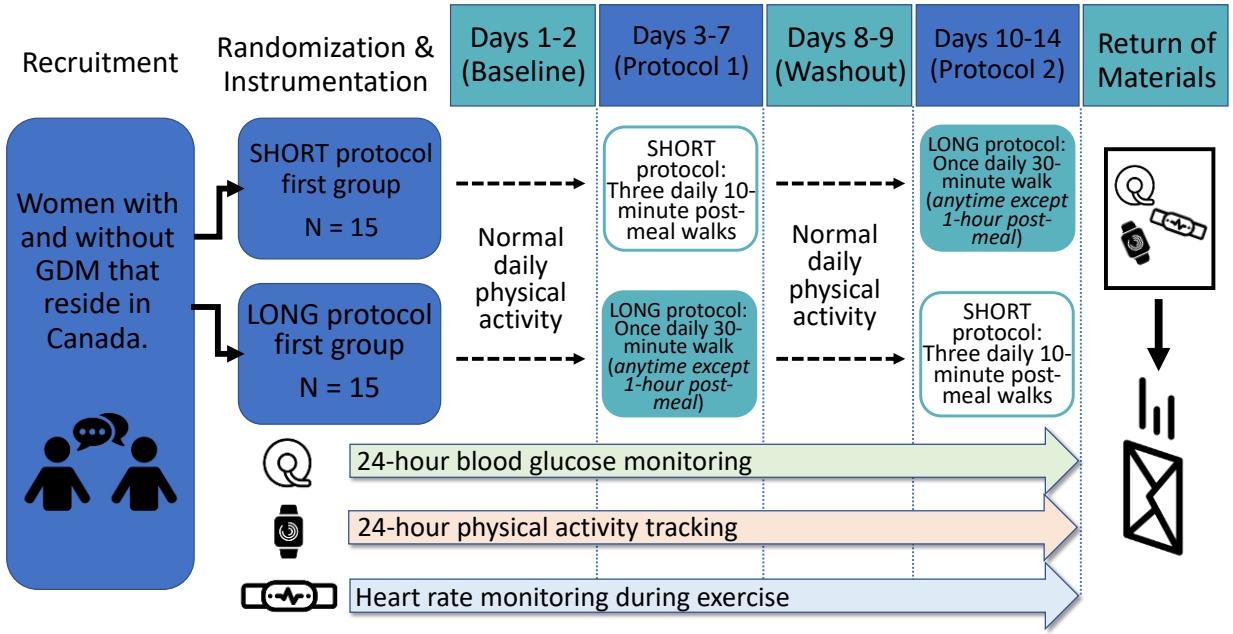
parity, and other health concerns. Participants completed the questionnaire in an online format via Redcap. The HHQ can be found in appendix A.

Participants were also asked to complete a Physical Activity Enjoyment Scale (PACES), which assesses the extent to which individuals enjoy or dislike participating in any given physical activity. This scale has previously been assessed, and is a reliable and valid tool for the assessment of enjoyment of physical activity. [110,111] This questionnaire asks participants to select a ranking on a scale of one to seven between two opposing statements such as "I enjoy it" and "I hate it". There are 18 total rankings to be chosen. The rankings are added up to give the participants' final scores out of a maximum of 126. A lower score would suggest low enjoyment of the given activity, and a higher score would suggest more enjoyment. Participants were asked to complete the questionnaire twice; once at the end of Day 7 and once at the end of Day 14 to compare enjoyment of each condition. The PACES questionnaire can be found in appendix B.

COVID-19 Modifications

Due to COVID-19, all recruitment and participation occurred remotely. Those interested in participating contacted the researchers and a phone or video appointment was set up to discuss the study and obtain consent. All study materials (e.g., accelerometer, FGM) were handled with gloved hands and cleaned with an anti-viral wipe (e.g., Lysol wipes) prior to being sent or dropped off to participants. Once received, participants notified the researchers to set up another call and initiate the study. When participant completed the study, materials were mailed back to the researchers in a pre-paid envelope.

Figure 2. Study design.



CHAPTER 4: ANALYSIS

Data Analysis

Glucose Outcomes

Data from the FGM devices was downloaded to Microsoft Excel files using the FreeStyle Libre Software Version 1.0 software and analyzed offline. Interstitial fluid glucose was measured and used as a proxy for blood glucose levels. The primary outcomes were 1 and 2 hour postprandial glucose values after the start of each meal (breakfast, lunch, dinner). Secondary outcomes included fasting (value upon awakening), mean 24-hour (midnight to midnight), peak and nadir glucose, time in target (3.3-7.8 mmol/L), time spent < 3.3 mmol/L, and time spent > 7.8 mmol/L. Daily mean 1 and 2 hour postprandial outcomes were calculated using days 1 to 5 of the SHORT condition and 2 to 5 of the LONG condition. Daily mean 24-hour, peak and nadir glucose, time in target, time < 3.3 mmol/L and > 7.8 mmol/L were calculated using days 2 to 5 of the first condition completed, and 2 to 4 of the second condition completed, as the glucose monitor stopped recording partway through the 14th day of the study period. The first day of each condition was excluded in order to not use data collected prior to exercise stimulus. While the FGM records interstitial fluid glucose values in five minute intervals, only 15 minute average blocks are able to be exported. In order to account for the delay between interstitial and blood glucose, a five minute shift was applied to glucose values. [112] Participants' values for each outcome within each condition (NORMAL, SHORT, LONG) were averaged and contributed to the groups' means.

Physical Activity

Accelerometers were used to measure physical activity throughout the day, and to confirm compliance to the interventions by participants. Due to technological error, no viable heart rate data was recorded, and thus accelerometry data was used to determine fulfillment of prescribed

activity. This was done through recording accelerations over 60-second time intervals (epoch). The data collected was used to evaluate durations (summed durations of accelerations) and intensity (magnitude of accelerations) of their physical activity, and caloric expenditure throughout waking wear time.[113] To determine intensity, Freedson accelerometer count ranges were used: sedentary (< 100 counts per minute [cpm]), light activity (100-1951 cpm) and moderate to vigorous physical activity ($\geq$ 1952 cpm). [114] Non-wear times were confirmed using activity logs. Variables of interest included active energy expenditure (kcals), average wear time per day, time spent sedentary, time spent in light, moderate, vigorous, and very vigorous intensity activity, and total time spent in physical activity. Values for each outcome within each condition were averaged and contributed to each group's means. Only days with > 600 mins of wear time were included.

Dietary Intake

Dietary intake was derived from participant's food intake records and entered into the Food Processor Program (ESHA Research, Salem, OR, USA). Variables of interest across conditions and between groups included mean daily caloric intake, protein, fat, and carbohydrate intake. Values for each outcome within each condition were averaged per participant and included four days for the NORMAL condition, and five days for each the SHORT and LONG conditions.

Physical Activity Enjoyment

Physical activity enjoyment was assessed using the Physical Activity Enjoyment Scale (PACES). [111] Participants' rankings of statements was summed to give them a total score out of a maximum of 126, and each score contributed to the groups' means.

Statistical Analysis

Sample Size Calculation

Avery and Walker (2001) found that low-intensity postprandial exercise resulted in a mean difference (±SD) in blood glucose of 0.3 ± 0.3 at 30 minutes post- exercise. [98] Based on these findings, we estimated that 12 women are required per group to observe a significant difference in postprandial blood glucose and have increased the required sample size by 20% to account for study withdrawal (80% power, $\alpha = 0.05$; G*Power v3.1.9). A total of 15 participants per group were needed to be recruited.

Statistical Methods

Descriptive statistics were calculated and an unpaired t-test was used to compare demographic data between the GDM and NON-GDM groups. The outcomes including glucose, physical activity, dietary intake from each condition (NORMAL, SHORT, and LONG) and group (GDM and NON-GDM) were compared using a 2-way repeated measures ANOVA (group by condition) and post hoc Holm-Sidak test (SigmaPlot 13, Systat Software Inc., San Jose, California, USA). Compliance to the intervention between groups and conditions was assessed from the accelerometry data also using a 2-way repeated measures ANOVA and Holm-Sidak test. PACES scores were analysed in an identical fashion. Outcomes within each group were compared between conditions, and outcomes between groups were also compared within each condition. Significance was accepted at $p < 0.05$.

CHAPTER 5: RESULTS

Participant demographics

The GDM and NON-GDM groups were not significantly different in age, parity, pre-pregnancy body mass, body mass at participation, height, or pre-pregnancy BMI. However, the GDM group was more advanced in gestation by 4 weeks and 5 days ($P = 0.037$) (Table 3). Other than one participant in the GDM group, no other participants had a previous history of GDM. Three participants were prescribed diet and/or exercise as GDM therapy, one was prescribed Metformin, and one nocturnal insulin. No participants reported adverse events in relation to physical activity, the FGM, or blood glucose levels.

Table 3. Participant demographics.

	GDM (n=5)	**NON-GDM (n=5)**	***P***
Age (years)	36±5	32±2	0.174
Gestational age at participation (weeks)	33.6±3.3	28.9±2.6	**0.037**
Parity	2.0±1.2	1.0±0.0	0.151
Pre-pregnancy body mass (kg)	70±10	66±19	0.684
Body mass at participation (kg)	76±9	75±15	0.810
Height (cm)	161±6	163±6	0.758
Pre-pregnancy BMI (kg/m^2)	26.9±4.1	24.8±6.2	0.549
Previous history of GDM [n (%)]	1 (20)	0 (0)	0.690
Ethnicity	1 Mauritian 1 Black/African American 3 Caucasian	1 Asian 1 Mixed (half Asian half Caucasian) 3 Caucasian	

Data presented as mean ± SD unless otherwise indicated. BMI, body mass index. Independent t-tests were used to determine statistical differences between groups for continuous data. Tests of two proportions were used to determine statistical differences between groups for dichotomous data.

Physical activity

NORMAL physical activity was not different between GDM and NON-GDM groups (see Table 4). Sedentary time was not different between GDM and NON-GDM or between conditions

within each group. Daily active energy expenditure was significantly higher during the SHORT and LONG days compared to NORMAL for both GDM and NON-GDM groups.

Table 4. Accelerometer wear and physical activity outcomes in women with and without GDM throughout the NORMAL, SHORT, and LONG conditions.

	GDM (n=5)			**NON-GDM (n=5)**		
	NORMAL	*SHORT*	*LONG*	*NORMAL*	*SHORT*	*LONG*
Active energy expenditure (kcals)	234 ± 76	338 ± 137†	355 ± 81†	322 ± 181	428 ± 243†	435 ± 252†
Wear time (mins)	803 ± 33	772 ± 39	777 ± 20	784 ± 52	806 ± 57	816 ± 92
Sedentary (mins)	571 ± 84	514 ± 83	516 ± 54	530 ± 69	531 ± 91	553 ± 89
Light (mins)	219 ± 68	236 ± 52	231 ± 58	233 ± 34	237 ± 44	219 ± 30
Moderate (mins)	13 ± 11	22 ± 17	20 ± 9*	21 ± 16	38 ± 17†	43 ± 17†
Vigorous (mins)	0 ± 0	1 ± 1	6 ± 10*	0 ± 0	1 ± 1	0 ± 0
Very vigorous (mins)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Total activity (mins)	232 ± 72	259 ± 68	257 ± 51	254 ± 30	275 ± 47	262 ± 34
Total activity vs. NORMAL (mins)	---	27 ± 68	25 ± 40	---	22±57	8 ± 61
Sedentary (%)	71 ± 9	66 ± 9	66 ± 8	67 ± 5	66 ± 7	68 ± 5
Light (%)	27 ± 9	31 ± 7	30 ± 7	30 ± 5	30 ± 7	27 ± 5
Moderate (%)	2 ± 1	3 ± 2	3 ± 1*	3 ± 2	5 ± 2	5 ± 2†
Vigorous (%)	0 ± 0	0 ± 0	1 ± 1*	0 ± 0	0 ± 0	0 ± 0
Very vigorous (%)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0

Data presented as daily mean ± SD. Wear time, total time accelerometer was worn during waking hours; sedentary, time or % of wear time spent sedentary; light, time or % spent in light intensity physical activity; moderate, time or % spent in moderate intensity physical activity; vigorous, time or % spent in vigorous intensity physical activity; very vigorous, time or % spent in very vigorous intensity physical activity; total activity, sum of light, moderate, vigorous, and very vigorous intensity activity minutes. A two-way repeated measures ANOVA was used to determine statistical differences between groups.

† = statistically significant difference from the NORMAL condition, $P < 0.05$.

* = statistically significant difference from the NON-GDM group, $P < 0.05$.

During the SHORT condition, the GDM group walked for slightly less time than the NON-GDM group ($P<0.05$) (see Table 5). There was no significant difference in total walk time between groups during SHORT ($P>0.05$). GDM had slightly less total active time during the SHORT condition compared to LONG and compared to NON-GDM SHORT ($P<0.05$).

Table 5. Physical activity outcomes during prescribed walking time in women with and without GDM throughout the SHORT and LONG conditions.

	GDM (n=5)		**NON-GDM (n=5)**	
	SHORT	*LONG*	*SHORT*	*LONG*
Active energy expenditure (kcals)	87.1 ± 49.9†	125.2 ± 58.2	149.9 ± 85	154.8 ± 80.5
Total walk time (mins)	28.9 ± 1.4*	30.4 ± 0.6	30.7 ± 1.3	31.4 ± 1.4
Sedentary (mins)	0.6 ± 1	0 ± 0	0.1 ± 0.1	0.8 ± 0.9
Light (mins)	18.4 ± 8.5	13 ± 12.3	7 ± 6.4	4.8 ± 6.3
Moderate (mins)	9.6 ± 9.4*	15.7 ± 10.5	23.4 ± 6.3	25.8 ± 7.4
Vigorous (mins)	0.4 ± 0.5	1.8 ± 3	0.2 ± 0.5	0.1 ± 0.1
Very vigorous (mins)	0 ± 0	0 ± 0	0 ± 0.1	0 ± 0
Total active time (mins)	28.4 ± 1.6†*	30.4 ± 0.6	30.6 ± 1.4	30.6 ± 1.6
Sedentary (%)	2 ± 3.4	0 ± 0	0.3 ± 0.4	2.4 ± 2.8
Light (%)	64.7 ± 31.2†*	42 ± 39.5	22.8 ± 21.3	15.6 ± 21
Moderate (%)	32.1 ± 30.5*	52.1 ± 35.1	76 ± 20.6	81.8 ± 23.2
Vigorous (%)	1.2 ± 1.8	5.8 ± 10.1	0.8 ± 1.8	0.2 ± 0.4
Very vigorous (%)	0 ± 0	0 ± 0	0.1 ± 0.3	0 ± 0
Total active time (%)	98 ± 3.4	100 ± 0	99.7 ± 0.4	97.6 ± 2.8

Data presented as daily mean ± SD. Total walk time, total minutes of walking; sedentary, time or % of walk time spent sedentary; light, time or % spent in light intensity physical activity; moderate, time or % spent in moderate intensity physical activity; vigorous, time or % spent in vigorous intensity physical activity; very vigorous, time or % spent in very vigorous intensity physical activity; total activity, time or % sum of light, moderate, vigorous, and very vigorous intensity

activity minutes. A two-way repeated measures ANOVA was used to determine statistical differences between groups.
† = statistically significant difference from the LONG condition, $P < 0.05$.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.

Dietary intake

There was a significant effect of group where caloric and carbohydrate intake over the entire study period was higher in the NON-GDM than GDM (see Table 6, P<0.05). Within groups, mean caloric and macronutrient intake was not different between conditions. Within the GDM group, calories consumed during lunch were significantly higher than breakfast (see Table 7, P<0.05). There was no statistically significant difference in calories consumed at dinner compared to breakfast, or in carbohydrates consumed at lunch or dinner compared to breakfast. Within the NON-GDM group, calories and carbohydrates consumed at dinner were higher than at breakfast, but were not significantly different between lunch and breakfast.

Table 6. Dietary intake in women with and without GDM throughout the NORMAL, SHORT, and LONG conditions.

	GDM (n=5)			**NON-GDM (n=5)**		
	NORMAL	*SHORT*	*LONG*	*NORMAL*	*SHORT*	*LONG*
kcals	2023 ± 499	1979 ± 302	2119 ± 433	2542 ± 479	2639 ± 821	2835 ± 624
Carbs (g)	201 ± 58*	213 ± 52*	231 ± 73*	325 ± 75	330 ± 97	348 ± 71
Fat (g)	99 ± 28	89 ± 16	98 ± 15	97 ± 20	122 ± 52	121 ± 42
Protein (g)	90 ± 23	88 ± 12	84 ± 11	100 ± 16	94 ± 22	98 ± 13

Data presented as daily mean ± SD. A two-way repeated measures ANOVA was used to determine statistical differences between groups.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.

Table 7. Caloric and macronutrient intake in women with and without GDM across breakfast, lunch, and dinner.

	GDM (n=5)			NON-GDM (n=5)		
	BREAKFAST	*LUNCH*	*DINNER*	*BREAKFAST*	*LUNCH*	*DINNER*
kcals	325 ± 79	529 ± 70†	502 ± 77*	486 ± 124	643 ± 212	751 ± 211†
Carbs (g)	37 ± 9*	49 ± 14	46 ± 10*	64 ± 12	69 ± 16	87 ± 26†§
Fat (g)	15 ± 5	24 ± 6	23 ± 3	19 ± 6	31 ± 18	29 ± 9
Protein (g)	13 ± 5	29 ± 6†	28 ± 9†	17 ± 7	23 ± 3	37 ± 12†§

Data presented as daily mean ± SD. A two-way repeated measures ANOVA was used to determine statistical differences between groups.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.
† = statistically significant difference from breakfast.
§ = statistically significant difference from lunch.

Glucose outcomes

Postprandial glucose outcomes

Postprandial glucose outcomes are listed in Table 8.

Post-breakfast glucose values

There was a significant effect of group where GDM had higher 1 and 2 hour postprandial blood glucose values than NON-GDM during NORMAL and SHORT (see Table 8, P<0.05). Postprandial blood glucose values were not influenced by SHORT or LONG exercise in the GDM or NON-GDM groups. However, 1 hour post-breakfast blood glucose values were not different between GDM and NON-GDM in the LONG condition. The 2 hour post-breakfast blood glucose values were not different between GDM and NON-GDM in the LONG and SHORT conditions.

Post-lunch glucose values

Within NORMAL, there was a significant effect of group by condition where GDM had higher 1 and 2 hour postprandial blood glucose values than NON-GDM at lunch (see Table 8, P<0.05). GDM also had higher 2 hour postprandial blood glucose values during SHORT and

LONG compared to NON-GDM. Within groups, SHORT or LONG exercise did not affect postprandial blood glucose values. However, 1 hour post-lunch blood glucose values were not different between GDM and NON-GDM in the SHORT, but not the LONG condition.

Post-dinner glucose values

There was a significant effect of group by condition where GDM had higher 1 hour post-dinner glucose values during NORMAL and LONG (see Table 8, $P<0.05$). GDM also had higher 2 hour post-dinner glucose values within LONG. There was no difference in 2 hour postprandial blood glucose between groups in NORMAL or SHORT. Within groups, postprandial blood glucose values were not influenced by SHORT or LONG exercise. However, 1 hour postprandial blood glucose values were not different between the two groups in the SHORT condition.

Table 8. 1h and 2h postprandial glucose values in women with and without GDM across three conditions.

	GDM			**NON-GDM**		
(mmol/L)	*NORMAL*	*SHORT*	*LONG*	*NORMAL*	*SHORT*	*LONG*
1h post breakfast	6.05 ± 1.01*	6.08 ± 1.18*	5.68 ± 0.19	4.64 ± 0.89	4.74 ± 0.68	4.99 ± 0.89
2h post breakfast	4.86 ± 0.70*	4.68 ± 0.46	4.51 ± 0.35	4.12 ± 0.61	4.13 ± 0.19	4.16 ± 0.78
1h post lunch	6.39 ± 1.11*	5.82 ± 0.36	5.99 ± 0.95*	5.17 ± 0.73	4.94 ± 0.85	4.87 ± 0.84
2h post lunch	5.55 ± 0.61*	5.24 ± 0.53*	5.47 ± 0.36*	4.9 ± 0.66	4.48 ± 0.30	4.42 ± 0.17
1h post dinner	6.09 ± 0.53*	5.6 ± 0.87	5.99 ± 0.39*	4.72 ± 0.93	4.92 ± 0.38	4.62 ± 0.72
2h post dinner	5.4 ± 0.84	5.24 ± 0.51	5.5 ± 0.43*	4.67 ± 0.86	5.04 ± 0.15	4.63 ± 0.18

Data presented as daily mean ± SD. 1h and 2h post meal, glucose value at 1h and 2h postprandial. A two-way repeated measures ANOVA was used to determine statistical differences between groups.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.

Daily glucose values (fasting, 24h, peak, nadir, time in target, time <3.3, time > 7.8)

There was a significant effect of group where fasting, 24 hour mean, and nadir glucose values were higher in the GDM than NON-GDM across all conditions (see Table 9, $P<0.05$). Within groups, fasting, 24 hour mean, and nadir glucose values were not influenced by SHORT or LONG exercise.

There was a significant effect of group where GDM had higher peak glucose values than NON-GDM during NORMAL (see Table 9, $P<0.05$). However, the values were not different between GDM and NON-GDM in the SHORT and LONG conditions. Within groups, peak blood glucose values were not influenced by SHORT or LONG exercise; however, time spent in hyperglycemia was lower during LONG within the GDM group ($P<0.05$).

Time in target (3.3 to 7.8 mmol/L) and time spent in hypoglycemia (<3.3 mmol/L) were not significantly different between GDM and NON-GDM in NORMAL and LONG (see Table 9, $P<0.05$). However, there was a significant effect of group where GDM spent more time in target and less time in hypoglycemia than NON-GDM in SHORT ($P<0.05$).

Table 9. Fasting, 24h, peak, and nadir values, and time in target, time below 3.3 mmol/L and above 7.8 mmol/L in women with and without GDM across three conditions.

	GDM			NON-GDM		
	NORMAL	*SHORT*	*LONG*	*NORMAL*	*SHORT*	*LONG*
Fasting (mmol/L)	4.41 ± 0.47*	4.33 ± 0.44*	4.37 ± 0.44*	3.53 ± 0.32	3.5 ± 0.42	3.46 ± 0.32
24h mean (mmol/L)	5.01 ± 0.53*	5.02 ± 0.56*	4.86 ± 0.33*	4.13 ± 0.29	4.18 ± 0.36	4.2 ± 0.33
Peak (mmol/L)	7.66 ± 0.79*	7.2 ± 1.00	7.24 ± 0.33	6.16 ± 1.06	6.25 ± 0.88	6.55 ± 0.94
Nadir (mmol/L)	3.65 ± 0.51*	3.71 ± 0.41*	3.61 ± 0.47*	2.93 ± 0.23	2.99 ± 0.41	2.99 ± 0.34
Time in target (mins)	1367 ± 42	1403 ± 41*	1400 ± 28	1307 ± 113	1253 ± 174	1326 ± 128
Time < 3.3 (mins)	32 ± 58	3 ± 7*	19 ± 19	133 ± 113	180 ± 179	108 ± 131
Time > 7.8 (mins)	32 ± 40	16 ± 29	5 ± 5†	2 ± 5	5 ± 8	6 ± 9

Data presented as daily mean ± SD. Fasting, glucose value immediately prior to awakening; 24h mean, midnight to midnight; peak, highest value recorded; nadir, lowest value recorded; time in target, minutes spent between 3.3 and 7.8 mmol/L; time < 3.3, minutes spent below 3.3 mmol/L; time > 7.8, minutes spent above 7.8 mmol/L. A two-way repeated measures ANOVA was used to determine statistical differences between groups.
† = statistically significant difference from the NORMAL condition, $P < 0.05$.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.

Physical activity enjoyment

Within SHORT, there was a significant effect of group where GDM had lower enjoyment scores than NON-GDM (see Table 10, P<0.05). There was no statistically significant difference in enjoyment scores between groups in LONG. Within groups, there was no difference in enjoyment scores between exercise conditions.

Table 10. Physical activity enjoyment scale (PACES) group scores from the three 10-minute walks (SHORT) condition and the 30-minute walk (LONG) condition in women with and without GDM.

	GDM (n=5)		**NON-GDM (n=5)**	
	SHORT	*LONG*	*SHORT*	*LONG*
PACES score	89 ± 19*	89 ± 9	110 ± 8	107 ± 15

Data presented as daily mean ± SD. Maximum score is 126, minimum score is 18.
* = statistically significant difference from the NON-GDM group, $P < 0.05$.

CHAPTER 6: DISCUSSION

The present study compared the influence of three 10-mins postprandial walks to one 30-mins walk on postprandial and 24h glucose outcomes in women with and without GDM. Due to the influence of the COVID-19 pandemic, we were unable to recruit enough participants to have an appropriately powered study. Nonetheless, these data provide important pilot data that will inform a larger study investigating the impact of timing of physical activity in women with GDM in the future.

Physical activity

Overall, we demonstrated an increase in physical activity on the SHORT and LONG exercise days, compared to baseline. Our data also demonstrated that the prescribed physical activity did not impact the amount of time spent sedentary the rest of the day. As expected, physical activity was increased in the SHORT and LONG days in both groups compared to NORMAL. All participants completed the prescribed exercise (confirmed by accelerometry and exercise logs); however, the overall daily increase on the exercise days compared to NORMAL was slightly less for SHORT (GDM 90%, NON-GDM 73% of the prescribed exercise), and LONG (GDM 83%, NON-GDM 27% of prescribed exercise). These data suggest there may have been a small reduction in incidental physical activity on the exercise days which may have obscured the possible influence of the prescribed exercise on glycemic control.

Dietary intake

As a front-line therapy for managing GDM, dietary intake is important in controlling blood glucose values. As such, GDM patients often receive dietary counselling and are advised to consume foods with lower glycemic indices and control their caloric intake. [49,50] Thus, it is unsurprising that across all conditions, women in the GDM group consumed significantly less

amounts of carbohydrates and calories compared to their counterparts. The conscious effort to reduce caloric and carbohydrate intake in the GDM group may have already helped blunt their glycemic response to a meal, and thus may hide the potential effect of postprandial timing of exercise.

Additionally, the difference in caloric and carbohydrate intake between breakfast and lunch and breakfast and dinner could have played a role in the different postprandial glucose values seen after breakfast across conditions. Previous research demonstrates that exercise has a dose-response relationship, and given that the metabolism of smaller doses of glucose is easier, the exercise might not have as strong an effect on the lesser amount of calories and carbohydrates consumed during breakfast. [103] While there was a difference between the two groups' caloric and carbohydrate intake, no significant differences within each group's caloric, carbohydrate, fat and protein intake across the three conditions reduces the possibility that dietary intake was responsible for within-group glucose variables of interest.

Postprandial glucose outcomes

As expected, women with GDM had elevated blood glucose values compared to non-GDM at the start of the study. Although neither group demonstrated an impact of exercise on glucose values, these data hint that with an appropriately powered study the exercise conditions may be effective at improving overall blood glucose control. These preliminary data demonstrated that exercise may be effective at lowering the 1 hour postprandial glucose concentrations of GDM patients to match that of a healthy pregnant population. The reduction in 1h post-lunch and dinner blood glucose values by postprandial exercise extends previous work by Garcia-Patterson et al. (2001), who found a 60-minute walk immediately following a meal to be effective at reducing 1 hour postprandial values in women with GDM. Importantly, our data suggest that shorter durations

of activity may also be effective at reducing 1 hour postprandial blood glucose levels in women with GDM. While the LONG condition appeared to be more beneficial for 1 hour post-breakfast glucose values, the SHORT condition was more successful at reducing the 1 hour postprandial values to become not significantly different from the group without GDM, as it did so for both lunch and dinner. There are several reasons as to why this might be, and to make a case as to why the timing of exercise might be important.

Lunch and dinner are typically larger, more calorie intensive meals, and thus more carbohydrate intensive, as was the case in this study. While we were underpowered for statistical within-group differences, values show that while the SHORT condition was most effective at normalizing 1 hour post-lunch and dinner glucose values, this was not so for post-breakfast values. We speculate that the lower caloric and carbohydrate consumption associated with breakfast may have been easier to metabolise compared to lunch and dinner, and thus left little room for the effect of timing on postprandial values.

The effect of the SHORT condition on 1 hour post-lunch and dinner glucose values likely is related to the relationship between muscle activation during exercise and glucose uptake. Previous research has shown that acute bouts of exercise in women with and without GDM effect a reduction in circulating blood glucose both during and following exercise, however the timing around meals has not been controlled. [103] Exercise promotes increased glucose delivery to the working muscle, as well as the translocation of an insulin-regulated glucose transporter to the sarcolemma and t-tubules of contracting muscle. [115] Thus, it is reasonable to suggest that exercise-stimulated glucose uptake during the postprandial period of rising glucose values would be an effective way to blunt the glycemic response to meals. Additionally, regularly exercising following larger meals with a higher glycemic index could also improve overall daily glycemic control.

While there are precedents for the success of the SHORT condition in improving 1 hour postprandial glucose values in women with GDM, previous work corroborates the findings that the LONG condition, (exercise performed outside of the hour after meals) was not as effective in improving these values. Lesser et al. (1996) investigated the effect of one 30-minute bout of moderate intensity on postprandial blood glucose levels the following day (14 hours post-exercise) in women with GDM. [97] Results indicated that this amount of exercise was not successful at improving postprandial glycemic excursion. Similar observations were made in the present study, where the LONG condition consisting of once per day, 30-minute walks did not manage to improve 1 hour post lunch or dinner glucose values in the same day, perhaps because they did not occur immediately following meals.

Although results from this pilot study suggest that the prescription and timing of exercise may impact 1 hour postprandial blood glucose values, they also suggest that the amount and timing of exercise was not as important in exerting change on the 2 hour postprandial glucose values. Previous research by Avery and Walker (2001) found that the effects of exercise on blood glucose levels in women with GDM does not extend past 45 minutes post-exercise. [98] Participants in their study rested or exercised for 30 minutes at low or moderate intensities and had blood samples taken every 15 minutes from the start of exercise until 45 minutes post-exercise. Even with 30 minutes of moderate intensity activity, no improvement in blood glucose was observed past 45 minutes post-exercise; thus, it is likely that the duration and intensity of our 10-minute exercise bouts were not enough to influence 2 hour postprandial blood glucose values, given that Avery and Walker (2001) did not find an effect with their more robust exercise prescription past 45 minutes. In order to attempt to see a change in 2 hour postprandial values, longer and more intense exercise bouts, or perhaps a longer duration of intervention would likely be required.

The present study did not see any statistically significant differences in 1 and 2 hour postprandial glucose levels within groups. However, the mean glucose values in the exercise groups were reduced suggesting that with an appropriately powered study, the exercise conditions may be effective at improving these values. Within the 1 and 2 hour postprandial glucose levels, we see a 0.5 mmol/L and 0.2 mmol/L respective reduction in the SHORT compared to NORMAL condition in the GDM group. These reductions, especially concerning the 1 h postprandial value, could be clinically meaningful and important for the way healthcare providers prescribe exercise to patients with GDM. With a greater sample size, we may indeed see that the timing of exercise is important for postprandial glycemic control.

Daily glucose outcomes

As expected, the GDM group had elevated fasting, 24h mean, peak, and nadir glucose values compared to the NON-GDM group at baseline. While fasting, 24h mean, and nadir glucose values all remained significantly elevated in the GDM compared to NON-GDM, results showed that both exercise conditions were effective at reducing peak glucose values in women with GDM to be comparable with that of the healthy pregnant population. This could be attributed to the effect of chronicity of exercise, previous research having demonstrated that regular exercise in women with GDM improves glycemic control compared to non-exercising counterparts. [103]

However, while chronic exercise may have shown an effect of group by condition in some measures, it is possible that the length of the intervention, and the duration and/or intensity of the exercise bouts of the present intervention was not enough to show within-group effects. Studies that show a reduction in fasting and 24h blood glucose levels in pregnant women with or without GDM typically take place over a much longer period of time, generally about 6 weeks minimum. [88,91,116] Perhaps more intense exercise would have shown greater reductions in peak glucose, time

> 7.8 mmol/L, and postprandial values, which would in turn contribute to a lower overall 24h mean value.

In the present study, the only change in glycemic control observed within groups was in the GDM group, with the reduction time > 7.8 mmol/L in the LONG condition compared to NORMAL. This phenomenon was not observed of the SHORT condition, which may have been affected by the greater proportion of vigorous intensity physical activity in the LONG compared to the SHORT condition. No other values within groups were significantly different, and while this could be due to the small sample size, it is also possible that greater effects would have presented themselves had the there been a larger difference in active minutes between the exercise conditions and NORMAL. It is known that exercise has a dose-response relationship, and thus, increasing the discrepancy between active minutes during exercise conditions compared to NORMAL may show that timing of exercise is important. [103] This could especially have an effect because the SHORT condition already has such brief bouts of exercise, that a few minutes more may make a difference.

Although no adverse or symptomatic hypoglycemic events were reported in either group, study results indicated significantly more time spent in hypoglycemia (<3.3 mmol/L) in the NON-GDM group compared to the GDM group. This may be explained by the gradient between interstitial and plasma glucose concentrations of between 20% up to 110%. [117,118] As well, during times of decreasing glucose, interstitial glucose values may drop prior to plasma glucose, and may reach nadir values lower than the corresponding venous glucose values, especially during blood glucose values <3.3 mmol/L. [118,119] As with the present study, previous research has also shown substantial time (≥ 2 hours/day) spent in hypoglycemia within healthy pregnant individuals without adverse hypoglycemic events reported. [44,120] Though there is a significant amount of time

spent in hypoglycemia within the NON-GDM group and a discrepancy between the GDM and NON-GDM groups, these values are not likely to be clinically significant give that NON-GDM participants were not experiencing hypoglycemic symptoms and were not on medications to lower blood glucose levels. Additionally, while hypoglycemia during pregnancy is defined as <3.3 mmol/L, it is difficult to establish an official lower limit of blood glucose during pregnancy due to the variability of hypoglycemia between people with and without diabetes, and the differences in symptoms, therapies, associated risk, and medical condition. [1,44,45]

Physical activity enjoyment

Results of the physical activity enjoyment scale indicate that within each group, neither the three 10-minute walks nor the 30-minute walk was more enjoyable. While only the SHORT condition showed a statistically significant difference in enjoyment between groups, results suggest that overall the NON-GDM group enjoyed the physical activity prescribed more than the GDM group. Within both exercise conditions, the GDM group's scores indicates that on average they gave a ranking of 4 for each set of statements, compared to an average of 6 within the NON-GDM group. This may be due to the difference in gestational age and the physical changes that come along with later gestation, as the group with GDM was one month farther along in gestation than the NON-GDM group. It would be of importance to find a way to make the activity more enjoyable for women with GDM to ensure compliance to physical activity prescriptions, given that walking is a feasible, accessible, and low-cost activity, and that physical activity is important in glycemic control. [103,105]

Limitations

The objective of the present study was to determine the effect of two different timings of exercise on postprandial and 24h glucose outcomes among women with and without GDM. Based

on sample size calculations, a sample size of 12 per group (GDM and NON-GDM) would have been required to detect significant differences in values across conditions within each group. Although this study was underpowered to show a significant difference within each group, the analysis comparing the two groups supports a beneficial effect of the three 10-mins postprandial walk schedule for the group with GDM. Additionally, while caloric and carbohydrate intake was similar across all conditions within each group, not implementing standardized meals could mean that some postprandial values were affected by dietary compositions. It is also important to highlight that the 1 month difference in gestation between the GDM and NON-GDM groups may bias the results towards a greater difference in blood glucose values between the two groups, due to the progression of insulin resistance throughout gestation. Thus, the influence of the 10-minute walks may not be as pronounced in a group matched by gestation. [25,26] Lastly, it should be noted that the method of analysis may pose additional limitations. Daily 24 hour glucose data is excluded from the first day of each condition to avoid including values pre-stimulus, however, this may bias results towards a more effective intervention due to the chronic benefits and dose-response relationship of exercise. As well, missing the data after the FGM stops recording on the 14th day of the study period may hide the influence of chronic exercise and bias the results in the opposite direction.

Strengths

While previous research has demonstrated that exercise can chronically and acutely improve blood glucose levels, this is the first study to investigate whether the timing of exercise has any implication on both postprandial and glycemic control. While underpowered and unable to compare values between conditions within each group, we were still able to compare the GDM to NON-GDM group and investigate the effect of timing of exercise. Additionally, not using

standardized meals increased the external validity of the study by having participants participate in free-living conditions. This helps make the results more clinically meaningful and significant. Lastly, both exercise conditions are practical because walking is typically an accessible activity, using minimal equipment, and 30 total minutes per day is achievable in terms of time commitment compared to the 60 minutes walking condition investigated by Garcia-Patterson et al. (2001). [99]

Future directions

A future investigation with a larger sample size is needed to determine the effect of exercise timing within a sample of participants with GDM. With a larger sample size, future studies should also compare the effects of exercise timing between different GDM therapies (i.e. Metformin, insulin, diet controlled) and whether timing of exercise influences the amount of medication needed. Future research should also explore other modalities of exercise with varying intensities. Research is also needed to determine whether exercise timing could help prevent GDM, which would be clinically important for all pregnancies. Lastly, future research should examine whether the timing of exercise affects clinically significant outcomes in pregnancies affected by gestational diabetes.

CHAPTER 7: CONCLUSIONS

Based on the current sample size, shorter, more frequent bouts of exercise compared to one longer daily bout of exercise do not improve 1 and 2 hour postprandial glucose values, fasting, 24h mean, peak, and nadir values, time in target, time > 3.3 mmol/L or time > 7.8 mmol/L within a group of women with or without GDM. However, three 10-minute walks per day at a moderate intensity are more effective than one 30-minute walk per day at reducing 1 hour postprandial values in women with GDM to match values of a group of pregnant individuals without GDM. Results of the study also suggest that 150 mins of light-to-moderate intensity exercise spread over 5 days per week with either timing is effective at normalizing peak glucose values and time > 7.8 mmol/L within the GDM group.

To our knowledge, this is the first study to investigate the impact of timing of exercise around meals. It is of clinical relevance and importance to know if the timing of exercise matters, or whether what matters most for glycemic control is that the prescribed amount of exercise is fulfilled. This may potentially help healthcare providers better care for patients with gestational diabetes, and encourage individuals to meet physical activity guidelines in the manner that best suits them. Higher compliance to physical activity in pregnancies affected by GDM helps reduce blood glucose levels, and is essential to diminish risks of complications for mom and baby during pregnancy, birth, and beyond. [2–4,37,66–68]

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APPENDICES

Appendix A: Health History Questionnaire

Date of Birth: _____/_____/_____ Height: _____ Weight: _____

Due/Delivery Date: _____ Marital Status: _____

Section A – Background Information:

1) With which gender identity do you most identify?
□ Man □ Woman □ Non-binary □ Not listed/Other:_____
□ Prefer not to say

2) What is your ethnicity?
□ Asian □ Hispanic or Latinx
□ Black or African American □ Caucasian
□ First Nations, Métis, Inuit, American Indian, or Alaska Native (please specify):_____
□ Native Hawaiian or other Pacific Islander □ Mixed Heritage, please specify:_____
□ Other, please specify: _____ □ Unknown
□ Prefer not to say

3) What education level did you complete? Please check all that apply.
□ Elementary school □ High school □ College
□ University (please circle: certificate, bachelor, master, doctorate, professional degree [MD, DMD, DDS, Law, etc.])
□ Other, please specify_____
4) What is your occupation?_____

5) Approximately how many hours per week do you work? _____

Section B – Health History:

6) Personal history is related to your own health. Family history is related to the blood relatives of both you and your baby's father (i.e., maternal and paternal relatives). This includes:

- You/your baby's father's mother and father
- You/your baby's father's grandparents
- You/your baby's father's siblings
- You/your baby's father's other children
- You/your baby's father's aunts and uncles who are related by blood

Cardiovascular health history.
Please check any and all that apply:

	Personal History	Family History
Stroke	□	□
Hypertension	□	□
Heart Attack	□	□
Heart Murmur	□	□
Blood clots	□	□
Anemia	□	□
Congestive Heart Failure or Heart Failure	□	□
Other cardiovascular disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:

_____

Metabolic health history.
Please check any and all that apply.

	Personal History	Family History
Type I Diabetes	□	□
Type II Diabetes	□	□
Pre-diabetes/Impaired Glucose Tolerance	□	□
Polycystic Ovarian Syndrome	□	□
Categorized as Obese	□	□
Protein in Urine	□	□
Other metabolic disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:

_____

Respiratory health history.
Please check any and all that apply:

	Personal History	Family History
Asthma	□	□
Sleep Apnea	□	□
Chronic Obstructive Pulmonary Disorder (COPD)	□	□
Other respiratory/breathing disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:

_____

Neurological health history.
Please check any and all that apply:

	Personal History	Family History
Alzheimer's	□	□
Cognitive impairment	□	□
Parkinson's	□	□
ALS (Lou Gehrig's Disease)	□	□
Seizures	□	□
Epilepsy	□	□
Multiple Sclerosis	□	□
Depression	□	□
Other neurological disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:

_____

7) Other Health History Questions

	Yes	No
Any other major surgery, illness or injury not listed above? (If yes, please Specify)	□	□

_____

	Yes	No	Unknown
Were you born pre-mature (before 37wks)	□	□	□

(If yes, what week were you born?) _____

What is the year of birth of your Mother? _____

What is the year of birth of your Father? _____
What is your birth order? 1= first born, 2 = second born etc.
_____

	Yes	No
Do you smoke?	□	□

(If yes, how many cigarettes per day?)
_____

(If you have quit, how long since your last cigarette?)
_____

	Yes	No
Are you exposed to second-hand smoke?	□	□

Please indicate if at home or other. (If yes, where?) _____

	Yes	No
Do you drink caffeine regularly?	□	□

(Some examples of caffeinated beverages include: non-decaf coffee, brewed black/green tea, energy drinks, colas – like regular/diet Pepsi, regular/diet Coke, Mountain Dew, Dr. Pepper etc.)

What kind(s) of caffeinated beverages do you drink?
□ Coffee □ Energy drinks □ Tea □ Colas
□ Other: _____

How many cups of caffeinated beverages do you drink:
per day? _____
per week? _____

	Yes	No
Are you currently taking any medications?	□	□

(If yes, please list medications)
_____

_____

Do you have any other health concerns you think we should be aware of?
_____

8) MENSTRUAL STATUS AND PREGNANCY INFORMATION
These questions are for females only.

	Yes	No
Are you post-menopausal?	□	□

(If not, how long since your last period?)

_____

	Yes	No
Are you on hormone replacement therapy?	□	□

_____

	Yes	No
Are you currently using contraceptives?	□	□

(If yes, what method? Please select any and all that apply.)

□ Oral contraceptives (pill). Brand: _____
□ Intrauterine Device (IUD). Type (Copper or Hormonal): _____
□ Birth control impant
□ Birth control shot/injections (e.g. Depo-Provera)
□ Vaginal ring
□ Birth control patch
□ Physical barrier (condom, internal condom diaphragm, birth control sponge, cervical cap)
□ Spermicide
□ Other: _____
□ No, I am not currently using any contraceptives

	Yes	No
Are you pregnant?	□	□

(If yes, how many weeks?)

_____

Is your due date:

□ calculated from the date of your last period
□ confirmed by your ultrasound
□ not sure

	Yes	No
Is this your first pregnancy?	□	□

_____

How did you conceive this pregnancy?

□ Spontaneous (without the use of Assistive Reproductive Technology)
□ With help from Assistive Reproductive Technology (ART)

*Note: Assistive Reproductive Technology includes methods such as hormonal assistance, IVF, and others.

What method(s) of Assistive Reproductive Technology was used for this pregnancy?

_____

Please select any and all of the following that you have been diagnosed with in your current or previous pregnancy(ies):

	Yes	No
Gestational Diabetes Mellitus	□	□
Impaired Glucose Tolerance/Pre-diabetes	□	□
Gestational Hypertension	□	□
Preeclampsia	□	□
Eclampsia	□	□
Placenta Previa	□	□
Preterm Labour	□	□
High-order Pregnancy (ie. Twins, Triplets, or more)	□	□
Post-partum Depression	□	□
Post-partum Anxiety	□	□
Anxiety during pregnancy	□	□
Depression during pregnancy	□	□
Other, please specify: _____	□	□

Please indicate which pregnancy(ies) were affected:

_____

Was your mother diagnosed with any of the following during any of her pregnancies?

	Yes	Yes, while pregnant with me	No
Gestational Diabetes Mellitus	□	□	□
Impaired Glucose Tolerance/Pre-diabetes	□	□	□
Gestational Hypertension	□	□	□
Preeclampsia	□	□	□
Eclampsia	□	□	□
Placenta Previa	□	□	□
Preterm Labour	□	□	□
High-order Pregnancy (ie. Twins, Triplets, or more)	□	□	□
Post-partum Depression	□	□	□
Post-partum Anxiety	□	□	□
Anxiety during pregnancy	□	□	□
Depression during pregnancy	□	□	□
Other, please specify: _____	□	□	□

_____

Section C – Nutrition, Physical Activity and Sleep:

9) What have your eating habits been like in the year before this pregnancy? Check all that apply.:

□ One meal per day, specify when _____
□ Two meals per day, specify when _____
□ Three meals per day
□ Snack(s) every day, specify when _____
□ Special diet, please specify name _____
□ Trying to follow Canada's Food Guide to Healthy Eating
□ Other nutrition plan, please specify _____

10) What have your eating habits been like in the during this pregnancy? Check all that apply.:

□ One meal per day, specify when _____
□ Two meals per day, specify when _____
□ Three meals per day
□ Snack(s) every day, specify when _____
□ Special diet, please specify name _____
□ Trying to follow Canada's Food Guide to Healthy Eating
□ Other nutrition plan, please specify _____

11) What was your pattern of physical activity in the year before this pregnancy?
This question also applies to non-pregnant women and women >12 months postpartum

Type of Physical Activity (e.g. walking, swimming, cycling etc.)	Frequency (average time(s) per week, e.g. if 3-5, put 4)	Average Duration of your exercise sessions (in minutes)	Intensity (light, moderate or strenuous)	Location (home, outdoors, gym, etc.)
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		

DEFINITIONS:
Light Intensity (minimal effort; e.g. yoga, easy walking, golf, bowling, stretching).
Moderate Intensity (not exhausting; e.g. fast walking, baseball, tennis, easy bicycling)
Strenuous Intensity (heart beats rapidly; e.g. running, jogging, vigorous swimming, vigorous long distance cycling).

12) During a typical 7-Day period (a week) in the year before this pregnancy, in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?
This question also applies to non-pregnant women and women >12 months postpartum

□ often

□ sometimes

□ never/rarely

13) What was/is your pattern of physical activity been like during this pregnancy?

Type of Physical Activity (e.g. walking, swimming, cycling etc.)	Frequency (average time(s) per week, e.g. if 3-5, put 4)	Average Duration of your exercise sessions (in minutes)	Intensity (light, moderate or strenuous)	Location (home, outdoors, gym, etc.)
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		
	_____ time(s) per week	_____ minutes		

14) During a typical 7-Day period (a week) during this pregnancy, in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

□ often

□ sometimes

□ never/rarely

15) During this pregnancy, were you ever prescribed to restrict your activity levels by a healthcare provider? Restricting activity would mean avoiding specific activities like exercise, walking, and/or sexual activity. This may have been called bed rest.

Yes □ No □

15a) If yes, what kind of activity restriction(s) were you prescribed? Select all that apply.

□ Restrict you physical activity intensity, duration, or frequency
□ Avoid physical activity
□ Be on pelvic rest (e.g. avoidance of lower body exercise or sexual activity)
□ Avoid all activity apart from walking to the washroom
□ Other activity restriction, please explain: _____

15b) Do you know why you were prescribed this activity restriction?

□ Yes, because _____
□ No, I don't know

□ No, I don't remember
□ Other, please explain: _____

15c) Please indicate during which week of pregnancy you were prescribed the activity restriction(s):

_____

16) What is/was your level of stress on most days (please check one box for each time point) ?

Timepoint	No stress	Low Stress level	Moderate stress level	High stress level
In the year before your current pregnancy.				
During your current pregnancy.				
After your current pregnancy.				
Non-Pregnant or >12 months postpartum				

Section D – Previous Pregnancies:

17) What has been your usual adult body weight? _____ pounds, OR _____ kg

18) What was your body weight one year before this pregnancy?_____ pounds, OR _____ kg

19) What was your body weight immediately before this pregnancy? _____ pounds, OR _____ kg

20) How much weight do you or did you plan to gain during this pregnancy?
_____ pounds, OR _____ kg
21) How much weight did you gain during this pregnancy?

_____ pounds, OR _____ kg

22) Did your health care provider tell you how much weight you should gain during your pregnancy?
□ No □ If Yes, how much weight were you told? _____ pounds, OR _____ kg

23) Were you actively trying to reduce your body weight in the year before this pregnancy?
□ No □ If Yes, how much weight did you lose? _____ pounds, OR _____ kg

Section E – Previous Pregnancies:

24) Please fill the following chart.

	Age you were	Body weight you were immediately before pregnancy	Weight you gained during pregnancy	Weight retained after pregnancy (never really lost)
1st pregnancy		_____pounds, OR _____kg	_____pounds, OR _____kg	_____pounds, OR _____kg
2nd pregnancy		_____pounds, OR _____kg	_____pounds, OR _____kg	_____pounds, OR _____kg
3rd pregnancy		_____pounds, OR _____kg	_____pounds, OR _____kg	_____pounds, OR _____kg
4th pregnancy		_____pounds, OR _____kg	_____pounds, OR _____kg	_____pounds, OR _____kg
5th pregnancy		_____pounds, OR _____kg	_____pounds, OR _____kg	_____pounds, OR _____kg

25) For each pregnancy, what were the gestational age, gender and approximate birth weight and length?

	Gestational Age	Sex (Male, Female, or Intersex)	Birth Weight	Birth Length
1st baby	_____ weeks		_____pounds _____ounces, OR _____kg	_____inches, OR _____cm
2nd baby	_____ weeks		_____pounds _____ounces, OR _____kg	_____inches, OR _____cm
3rd baby	_____ weeks		_____pounds _____ounces, OR _____kg	_____inches, OR _____cm
4th baby	_____ weeks		_____pounds _____ounces, OR _____kg	_____inches, OR _____cm
5th baby	_____ weeks		_____pounds _____ounces, OR _____kg	_____inches, OR _____cm

26) Please indicate how you fed your baby(ies).

	Breastfeeding initiated?	Duration of breastfeeding only	Age breastfeeding was stopped	Age at introduction of first solid foods
1st baby	____ Yes, ____ No	_____ months	_____ months	_____ months

2nd baby	____ Yes, ____ No	_____ months	_____ months	_____ months
3rd baby	____ Yes, ____ No	_____ months	_____ months	_____ months
4th baby	____ Yes, ____ No	_____ months	_____ months	_____ months
5th baby	____ Yes, ____ No	_____ months	_____ months	_____ months

Section F – Weight History:

27) What was your birth weight? _____ pounds _____ ounces, OR _____ kg

28) What was your birth length? _____ inches, OR _____ centimeters

29) What was the birth weight of the father of your child? ____ pounds _____ ounces, OR ____ kg

30) What was the birth length of the father of your child? _____ inches, OR _____ centimeters

31) How has your body weight been since you were 19 years of age?
 stable (always about the same weight, only changing by a couple of pounds when I am not pregnant), please skip to question 28
 unstable and progressively increasing
 unstable, because it has been going up and down often
 unstable, I feel I have been gaining weight with each pregnancy
 Other, please describe
_____

32) Have you ever had an eating disorder?
 Anorexia
 Bulimia
 Binge eating
 Disordered eating (Disordered eating describes a variety of abnormal eating behaviours that, by themselves, do not warrant a diagnosis or an eating disorder.)
 Other, please specify _____
 No eating disorder

33) What is the current status of your eating disorder?
 Recovered (i.e. no symptoms)
 Managed (i.e. some symptoms but controlled)
 Currently experiencing symptoms

□ Other: _____

Appendix B: Physical Activity Enjoyment Scale (PACES)

Participant ID: _____ Date:_____

Physical Activity Enjoyment Scale

Please rate how you feel *at the moment* about the physical activity you have been doing.
Indicate how much you agree with each statement set, on a scale of 1 to 7.
1 = strongly agree with first statement in the set / strongly disagree with the second statement
7 = strongly agree with the second statement in the set / strongly disagree with the first statement
For example, if you neither enjoyed nor hated the physical activity, you would select '4' for the first statement set. If you enjoyed it very much, you would select '1'.

	1	2	3	4	5	6	7	
I enjoy it								I hate it
	1	2	3	4	5	6	7	
I feel bored								I feel interested
	1	2	3	4	5	6	7	
I dislike it								I like it
	1	2	3	4	5	6	7	
I find it pleasurable								I find it unpleasurable
	1	2	3	4	5	6	7	
I am very absorbed in this activity								I am not at all absorbed in this activity
	1	2	3	4	5	6	7	
It's no fun at all								It's a lot of fun
	1	2	3	4	5	6	7	
I find it energizing								I find it tiring
	1	2	3	4	5	6	7	
It makes me depressed								It makes me happy
	1	2	3	4	5	6	7	
It's very pleasant								It's very unpleasant
	1	2	3	4	5	6	7	
I feel good physically while doing it								I feel bad physically while doing it
	1	2	3	4	5	6	7	
It's very invigorating								It's not at all invigorating

	1	2	3	4	5	6	7	
I am very frustrated by it								I am not at all frustrated by it
It's very gratifying	1	2	3	4	5	6	7	It's not at all gratifying
It's very exhilarating	1	2	3	4	5	6	7	It's not at all exhilarating
It's not at all stimulating	1	2	3	4	5	6	7	It's very stimulating
It gives me a strong sense of accomplishment	1	2	3	4	5	6	7	It does not give me any sense of accomplishment at all
It's very refreshing	1	2	3	4	5	6	7	It's not at all refreshing
I felt as though I would rather be doing something else	1	2	3	4	5	6	7	I felt as though there was nothing else I would rather be doing

Appendix C: Food log

Day 1 Food Intake Record. Date: _____

Meal	Location	Food Eaten	Amount	Condiment	Amount	Beverage	Amount
Breakfast Time:							
Snack Time:							
Lunch Time:							
Snack Time:							
Dinner Time:							
Snack Time:							
Additional meals/snacks Time:							

Overall, do you feel that the food choices and amounts you ate today were typical of your usual diet? □ Yes □ No

For the most part, when did you record the food items eaten?

□ Immediate after eating □ Awhile after eating □ At the end of the day □ Other: _____

Appendix D: Accelerometer wear and sleep log

Tracking:	**Day 1** **Date:** _____	**Day 2** **Date:** _____	**Day 3** **Date:** _____	**Day 4** **Date:** _____	**Day 5** **Date:** _____	**Day 6** **Date:** _____	**Day 7** **Date:** _____
Time you woke up							
Time device put on hips							
Time you went to bed							
Time device put on your wrist							
Time you went to sleep							
Please record your working hours EXAMPLE 8am – 4pm - Work							
Please record any time the device was off during the day and why EXAMPLE: 9am – 930am - Shower							
Please report any activities you did during the day and times you did them EXAMPLE: 6pm – 7pm - Yoga							
Please record any naps you took throughout the day EXAMPLE: 2pm – 230pm							