Glycemic Response to Acute High-Intensity Interval Training versus Moderate-Intensity Continuous Training during Pregnancy

by

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A Thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science

Faculty of Kinesiology, Sport and Recreation

University of Alberta

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Abstract

Moderate-intensity continuous training (MICT) continues to be the staple of prenatal physical activity research. The glucose lowering effects of MICT are well established with low risk of post-exercise hypoglycemia, however there is a large research gap concerning maternal response to short bursts of vigorous-intensities. Despite the growing number of individuals continue to participate in high-intensity interval training (HIIT) following conception, pregnant individuals glycemic response to HIIT has only been reported once with pre to post exercise capillary glucose samples. Since glucose is essential to supporting the maternal physiological adaptations to prepare the body for the demands of pregnancy and assist in fetal-placental growth, it is imperative to further investigate the glucose lowering effects of HIIT. Furthermore, the vast majority of vigorous-intensity research with pregnant populations has not exceeded 90% maternal HR_{max} and the effects on maternal glucose are essentially unknown. Therefore we sought to investigate maternal glycemic response during and following an acute bout of HIIT and MICT in pregnant individuals over a 48 hour period.

We recruited 24 pregnant females (27.8 ± 4.7 weeks of gestation, 31.5 ± 4.1 years of age) with a singleton pregnancy to participate in this randomized cross over design study. Each participant wore a flash glucose monitor and accelerometer, as well as kept a written food log, for seven days to collect 24 and 48 hour glucose values, physical activity patterns, and caloric intake. The participants engaged in two acute bouts of exercise (i.e., one HIIT and MICT session) in random order separated by 48 hours. The HIIT protocol consisted of 10 one minute intervals of high-intensity work (i.e., $\geq$ 90% HR_{max}) interspersed with nine one minute intervals of active recovery (19 minutes total). The MICT protocol consisted of 30 minutes of moderate-intensity cycling (i.e., 64 – 76% HR_{max}). Post-exercise participants were asked to report their perceived enjoyment and overall preference for HIIT or MICT. During the HIIT protocol, participants achieved peak heart rates of 159 - 185 bpm (85 - 97% of HR_{max}) with an average heart rate throughout the HIIT session (155 ± 8 bpm; 82 ± 4% HR_{max}) being significantly higher than during MICT (140 ± 8 bpm; 74 ± 4% HR_{max}; $P < 0.0001$). The change in glucose from pre to post exercise were not significantly different between conditions (HIIT: 0.62 ± 1.00 mmol/L; MICT: 0.81± 1.05 mmol/L; P = 0.30) with the exception that fewer individuals experienced post-exercise hypoglycemia after HIIT compared to MICT (8% versus 33% respectively; P = 0.04). All other glucose variables were not different between exercise protocols including mean 24 and 48 hour glucose, or time spent < 3.3 mmol/L or ≥ 7.8 mmol/L. Physical activity patterns (sedentary time, light, and moderate to vigorous intensity physical activity) and caloric intake (macronutrients and total calories) were not different between conditions or days. In comparison to MICT, HIIT was preferred by the majority of participants (87.5%). Sleep time following HIIT was 52 ± 73 minutes longer than the night before the HIIT session, while sleep after engaging in MICT was not changed. To our knowledge, this study is the first to report on the 48 hour glycemic response to aerobic HIIT with pregnant populations. Overall, an acute session of HIIT had no adverse effects on maternal glycemic response and elicited higher levels of perceived enjoyment in comparison to MICT. Results from this study improve healthcare provider and participant understand of the effects of HIIT. Future research is necessary to determine the effect of HIIT on fetal response as well as in individuals diagnosed with metabolic disorders such as gestational diabetes mellitus.

***Keywords**:* Glucose, Pregnancy, Pregnant, Exercise, High Intensity Interval Training, Moderate Intensity Continuous Training, Hypoglycemia, Cycling, Flash Glucose Monitor, Aerobic

Preface

The present thesis is original work created by Jenna B. Wowdzia. No part of this thesis has been published previously. Ethics approval was granted from the University of Alberta Research Ethics Board on November 16th, 2020, under the project name "Effects of acute high-intensity intervals versus moderate-intensity continuous cycling on maternal and fetal health" (Pro-00103630).

Jenna Wowdzia, Dr. Tom Hazell and Dr. Margie Davenport contributed to the design, acquisition, analysis and interpretation.

Acknowledgements

Special thanks to the Alberta Graduate Excellence Scholarship and the KSR Graduate Completion Scholarship for funding during my Masters of Science Degree.

I would like to express my deepest appreciation and thanks to Dr. Margie Davenport for her invaluable guidance throughout the process of my degree, as well as for her contribution and support on this paper. Thank you for always encouraging my curiosity and passions, as well as being an exemplary mentor. Thank you to Dr. Tom Hazell for your input on shaping this project and challenging me to explore different perspectives.

To my colleagues and classmates, thank you for all of coffee runs, late night writing sessions and for being such great supports throughout my degree. You shaped my academic journey into a wonderful and amazing adventure. Special thanks to Emily Vanden Berg, Dr. Aine Brislane and other colleagues/volunteers who helped me throughout my data collection process.

Importantly, thank you to all of the research participants whom made my research possible. Without your curiosity this project would never have been completed. I appreciated the joy you brought into our exercise sessions and your shared interest in our research.

Thank you to my family and friends that have consistently listened to me discuss my research and for lending an understanding ear during stressful times. Your unwavering support and encouragement have meant more to me than I can put into words. To my best friends, thank you for joining me on my crazy adventures and never questioning why my laptop joined us on so many of them. I will always cherish these moments.

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Glossary of Terms

ACSM	American College of Sports Medicine
BMI	Body Mass Index
CEP	Clinical Exercise Physiologist
CSEP	Canadian Society for Exercise Physiology
GDM	Gestational Diabetes Mellitus
GLUT4	Glucose transporter type 4
hPL	Human Placental Lactogen hormone
HIIT	High-intensity interval training
hPL	Human Placenta Lactogen
HR_{max}	Maximum heart rate
HRR	Heart rate reserve
IOM	Institute of Medicine
MICT	Moderate intensity continuous training
MVPA	Moderate to Vigorous Physical Activity
NEAT	Non-exercise Activity Thermogenesis
PACES	Physical Activity Enjoyment Scale
PARmed-X	Physical Activity Readiness Medical Examination
PSQI	Pittsburg Sleep Quality Index
REDCap	Research electronic data capture
RPE	Rating of Perceived Exertion
SGLT-1	Sodium Glucose Transporter

SOGC	Society of Obstetricians and Gynaecologists of Canada
VO_{2max}	Maximal oxygen consumption
VO_{2peak}	Peak oxygen consumption
VO_{2R}	Oxygen uptake reserve
WASO	Wake time after sleep onset

Chapter 1: Introduction

Significance

Moderate-intensity continuous training (i.e. 64 – 76% HR_{max}; MICT) is the staple of prenatal physical activity research [1–3]. Guidelines from around the world recommend that pregnant individuals participate in 150 minutes of moderate-intensity physical activity each week to achieve clinically meaningful health benefits [1–3]. These benefits include a 32% reduction in the odds of having excessive gestational weight gain [4], ~ 40% decline in the odds of developing gestational diabetes mellitus (GDM), preeclampsia and gestational hypertension [5], a 24% lower odds of instrumental delivery (i.e. forceps or vacuum) [6] and a 39% decrease in odds of having a fetal birthweight greater than 4,000 g (i.e. macrosomia) [7]. These health benefits are achieved without increasing the odds of preterm delivery, low birthweight, increased duration of labour, caesarean sections, or vaginal tears [6,7] . However, the current guidelines are limited as a result of the paucity of available data regarding the effects of higher intensities and specific types of exercise training during pregnancy. Individuals assume a level of risk when training beyond current guidelines as these practices have yet to be supported as safe during pregnancy. It is imperative to understand the effects of different types of prenatal physical activity, such as high-intensity interval training (HIIT), as an abundance of advice columns and prenatal workouts continue to be developed in the absence of scientific evidence [8].

HIIT has consistently ranked as a top five fitness trend from 2014 – 2021 [9]. HIIT consists of work intervals completed at intensities ≥ 80% HR_{max} interspersed with periods of lower intensity recovery or rest [10]. In non-pregnant populations, HIIT is effective at improving aerobic fitness (e.g. increase in VO_{2max} [11–13]), metabolic (e.g. greater insulin sensitivity [13]) and cardiovascular health (e.g. endothelial and ventricle function [11,12]). Despite the positive health benefits in non-pregnant populations, there has only been two studies investigating HIIT during human pregnancy. Utilizing a resistance based HIIT circuit targeting 80 – 90% maternal HR_{max}, investigators examined fetal wellbeing (heart rate and pre and post exercise umbilical artery indices [i.e. systolic/diastolic ratio, resistance index, and pulsatility index]) and did not identify any adverse effects [14]; thus demonstrating the feasibility of performing HIIT with pregnant populations and providing initial insight into the safety of HIIT in acute settings. Although the glucose lowering effects of MICT are well established [15], maternal glycemic response to HIIT remains essentially unknown. Ong and colleagues compared 20 minutes of MICT (i.e. 65% HR_{max}) to 21.5 minutes of HIIT [i.e., six 15 second self-paced work intervals interspersed with three minutes of moderate-intensity cycling (i.e. 65% HR_{max})] [16]. Investigators reported maternal glycemic response with capillary glucose samples at pre and post exercise were similar between exercise conditions (1.1 ± 0.2 mmol/L for MICT versus 1.0 ± 0.3 mmol/L for HIIT) with no reports of post-exercise hypoglycemia [16]. While this data is supportive of the safety of HIIT on maternal glycemic response, further research is necessary to determine the effects of longer duration work intervals and higher target heart rates. Addressing these gaps can aid in understanding the glucose lowering effects of HIIT.

During pregnancy an individual will experience a median decrease in maternal fasting plasma glucose of approximately 0.3 mmol/L compared to pre-conception levels [17]. The decline in circulating glucose is multifactorial as a result of the increased metabolic costs of supporting the pregnancy including the maternal physiological adaptations (e.g., adipose tissue deposition, increased blood volume) and the addition of the fetal-placental unit [17,18]. Maintaining an adequate supply of maternal glucose is essential for the growth and development of the fetus. In order to counteract the progressive decline in maternal glucose, an individual’s sensitivity to insulin decreases meaning they have a reduced ability to uptake circulating glucose from the blood into the skeletal muscle via insulin mediated pathways [19]. However, the non-insulin mediated glucose pathways stimulated with skeletal muscle contraction remains intact [20]. A recent meta-analysis illustrated that low to vigorous intensity physical activity is associated with a reduction in maternal blood glucose of 0.6 mmol/L but a low risk (i.e., 0 – 4%) of inducing post-exercise hypoglycaemia (< 3.3 mmol/L) [15]. The meta-regression analysis also demonstrated that as exercise intensities and/or durations increases, there is a dose response reduction in maternal glucose. Thus these findings suggest that higher intensities, such as obtained during aerobic HIIT (i.e., $\geq$ 90% HR_{max}), will increase the risk of maternal post-exercise hypoglycemia when compared to equivalent durations of MICT. However, HIIT is conventionally performed at shorter durations than MICT as it requires 40% less time commitment to achieve similar health benefits [21]. A longitudinal study in non-pregnant type two diabetics compared the glycemic effects of 45 minute MICT (i.e. 60% HRR) to 20 minutes of HIIT (i.e., six 60 second work intervals at 90% HRR interspersed with 2 minutes of recovery at 45% HRR) [22]. At 12 weeks of training the HIIT group demonstrating lower 24 hour and peak glucose levels, in addition to less time spent hyperglycemic compared individuals in the MICT group [22]. Acutely, HIIT (i.e., ten 60 second work intervals at $\geq$ 90% HR_{max} interspersed with 60 seconds of active recovery) has also demonstrated lower 24 hour average glucose, less time spent hyperglycemic and no reports of hypoglycemia in non-pregnant individuals with type two diabetes [23]. Thus it is reasonable to suggest, given an adequate training stimuli, HIIT has the potential to decrease glucose in acute and chronic settings. It is important to investigate the transferability of these findings to non-diabetic pregnant individuals to determine the possible effects of HIIT maternal glycemic response.

Purpose

The objective of this study was to investigate the glycemic response during pregnancy to an acute bout of aerobic HIIT and compare it to the recommended form of prenatal physical activity, MICT.

Delimitations

Twenty-four individuals with a singleton pregnancy, $\geq$ 18 years of age, $\geq$ 20 weeks gestation and did not have a diagnosis of a respiratory, cardiovascular, metabolic or neurological disorder were recruited for this randomized cross-over controlled trial. All volunteers were screened for absolute (e.g. ruptured membrane, pregnancy induced hypertension or pre-eclampsia, intrauterine growth restriction) and relative contraindications (e.g. history of spontaneous abortion, anemia, eating disorders) to prenatal physical activity using the PARmed-X for Pregnancy [24].

Volunteers wore a flash glucose monitor for seven days, allowing for 48 hour collection periods following each exercise test. Interstitial fluid glucose was used as a proxy for blood glucose levels and was monitored to assess: (1) the glycemic response from pre to post exercise and (2) the glycemic response over the subsequent 24 and 48 hours starting from the point at which their standardized snack was consumed approximately one hour prior to exercise. Physical activity and sleep were monitored using an activity monitor [i.e., Actigraph (ActiGraph LLC, Pensacola, FL)] and verified using a physical activity/sleep log. Nutrition was self-reported for seven days using a daily food log tracking sheet.

Limitations

This study refrained from testing participants before their 20th week of gestation, therefore the results are limited in their ability to address maternal response to HIIT throughout the entirety of pregnancy. In addition, a single bout of aerobic HIIT is unable to predict the cumulative effect of multiple sessions on maternal wellbeing. Due to the COVID-19 pandemic, participants were allowed to complete the exercise sessions from their home or at the Program for Pregnancy and Postpartum Health. This recruitment design allowed for greater inconsistencies (e.g., type/model of bike, unregulated environmental temperatures).

Primary Hypothesis

We hypothesized that:

(1) Maternal glucose would decrease from pre to post exercise in both the HIIT and MICT conditions;
(2) The magnitude of the decrease in maternal glucose from pre to post exercise would be greater with HIIT compared to MICT;
(3) 24 and 48 hour maternal glucose (starting from ingestion of the pre-test snack one hour prior to the acute bout of exercise) would be lower, but not hypoglycemic (< 3.3 mmol/L), for HIIT compared to MICT;
(4) The time spent hypoglycemic during the 24 and 48 hour periods would not be different between HIIT and MICT.

Secondary Hypothesis

We hypothesized that:

(1) Average and maximal intensity, as measured by maternal heart rate, would be greater during HIIT than MICT.
(2) Average, maximal, and overall session rating of perceived exertion (RPE) would be greater during HIIT than MICT.

(3) Metrics of physical activity, nutrition and sleep would not be dierent between HIIT and MICT.

Chapter 2: Literature Review

Pregnancy

A singleton pregnancy takes place over an average of 40 weeks (i.e., starting from the first day of a woman's last menstrual period and ending at fetal delivery) [25] and is broken down into three milestones called trimesters. The first trimester takes place over weeks 0 – 13, followed by the second trimester during weeks 14 – 27, and finally the third trimester from weeks 28 – 40. This is a period of significant physiological change where virtually all of the maternal organ systems adapt to support the demands of the growing fetus.

During pregnancy a number of physiological adaptations need to occur in order to support a healthy pregnancy. Weight gain is an expected response to pregnancy resulting from the growth of the fetal-placental unit, amniotic fluid, increased maternal blood volume (i.e., by approximately 45%) [26], an increase in maternal adipose tissue stores, as well as a number of other factors. The Institute of Medicine (IOM) recommend females of a normal pre-pregnancy body mass index (BMI; i.e., between 18.5 – 24.9 kg/m^2) gain between 25 – 35 lbs throughout pregnancy, with lower weight gain recommendations as pre-pregnancy BMI increases (i.e. 15 – 25 lbs for individuals classified as overweight; 11 – 20 lbs for individuals classified as obese) [27]. These recommendations are based on studies demonstrating weight gain within these ranges decreases the risk of pregnancy and delivery complications [28–30]. Gaining below the IOM recommendations is associated with increased risk of adverse pregnancy outcomes including low birthweight (< 2500 g) [29,30] and infant mortality [31]. Pregnancy weight gain above IOM's upper limit has also been associated with increased risk of having a macrosomic infant (birthweight > 4000 g) and cesarean deliveries [29,30]. Pregnant individuals also experience changes to their metabolic, respiratory and cardiovascular systems to ensure an adequate supply of oxygen and nutrients to the growing fetus. Although the adaptations to pregnancy are vast and multifaceted, the subsequent sections will focus on the adaptations most relevant to the current thesis.

Metabolic System

Glucose is a primary source of energy for humans and can be obtained through the consumption of carbohydrates [32]. The digestion of carbohydrates starts in the mouth where mechanical (i.e. chewing) and chemical (i.e. salivary amylase) processes help break them down into monosaccharides [32]. Monosaccharides, specifically glucose, are transported across the epithelium of the small intestine into the bloodstream by sodium glucose transporters (SGLT-1) located in the brush border [32]. Non-pregnant individuals without diabetes maintain their blood glucose between 4.0 mmol/L to 7.8 mmol/L [33]. In order to maintain a consistent level of circulating blood glucose, the body monitors the constant rise and fall in blood glucose via beta cells [34]. Beta cells are located in the pancreas and produce the hormone insulin [34]. Insulin initiates the pathway that transports glucose out of the bloodstream and into the tissues (e.g. adipose and muscle cells via GLUT4 transporter) for utilization and/or storage [34,35]. In the presence of high levels blood glucose, beta cells will produce and release insulin at an increased rate in order to achieve homeostasis [36]. Similarly, when experiencing low levels of blood glucose, the pancreas will reduce the production of insulin [36]. Low glucose triggers the alpha cells of the pancreas to produce the hormone glucagon [37]. Glucagon is responsible for sending signals to the liver which breaks down stored glycogen into glucose (i.e. the process of glycogenolysis) which is released into the circulation to raise blood glucose [38]. The combination of beta and alpha cells contribute to the homeostasis of glucose metabolism in the pregnant and non-pregnant state.

Fasting Glucose

Compared to pre-conception levels, females will experience a drop in fasting plasma glucose (i.e. median decrease of 0.1 – 0.2 mmol/L) during their first trimester [17,39] due to the expansion of maternal blood volume which dilutes its concentration concurrent with increased maternal metabolism [39–42]. During the first trimester the metabolic system begins to adapt by increasing the size and number of beta cells in the pancreas [43]. This results in increased insulin secretion (i.e. by 200 – 250% [44,45]) and greater levels of insulin sensitivity (i.e. the body's ability to uptake circulating insulin which aids in the removal of glucose out of the blood and into surrounding tissues [19]) during the first trimester [43]. These adaptations promote the uptake of glucose from the blood into maternal tissues, increasing energy storage in the adipose tissues, and preparing the body for the demands of pregnancy [18].

During the second trimester, maternal fasting plasma glucose stabilizes due to a decrease in insulin sensitivity at the skeletal muscle [39,46]. In the third trimester, the metabolic demands of the growing fetus increase such that further decreases in maternal insulin sensitivity are unable to maintain stable blood glucose [47]. Thus maternal glucose concentrations decline to levels ~ 0.3 mmol/L lower than preconception [41,42]. Glucose is the primary energy source for a growing fetus and it is dependent on the supply from maternal circulation [48]. In order to ensure adequate nutrition to both the pregnant individual and the fetus, placental hormones are released to promote the utilization of alternate energy sources by maternal tissues. During pregnancy the placenta produces the hormone human placental lactogen (hPL) from the syncytiotrophoblash cell layer [49]. hPL increases throughout pregnancy reaching its peak in the third trimester [49,50] and aids to ensure adequate supply of glucose to the fetus by decreasing maternal insulin sensitivity at the level of the skeletal muscle thereby decreasing maternal glucose utilization [41,42,49,50]. Due to these adaptations, a concentration gradient develops that favors the diffusion of glucose from maternal blood towards the fetus [49]. In response to hPL, maternal insulin secretion is also enhanced which promotes lipolysis (i.e. production of fatty free acids, ketones and triglycerides) [49,50]. Due to these physiological interactions, maternal metabolism becomes reliant on lipids ensuring adequate concentrations of glucose to be reserved for the fetus [49]. As a net result of metabolic adaptations, pregnancy hormones, decreased insulin sensitivity, and the growing glucose demands of the fetus, fasting plasma glucose levels are lower during pregnancy compared to pre-conception values [51].

Postprandial Glucose

After the consumption of food (i.e. postprandial period) pregnant individuals will experience an exaggerated increase in plasma glucose compared to their pre-conception levels [51]. A longitudinal study evaluating the glucose response to a standardized 75 g oral glucose tolerance test in 32 healthy individuals found their two hour postprandial glucose values increased during weeks 16 to 26 of pregnancy (5.3 mmol/L vs. 6.1 mmol/L, respectively) [52]. This rise postprandial glucose levels throughout pregnancy is considered normal and is a result of the progressive decline in insulin sensitivity and greater reliance on maternal lipid metabolism [49,51–

[53]. However, elevated postprandial glucose values are a key feature of the gestational diabetes mellitus (GDM). Defined as glucose intolerance with first recognition or diagnosis during pregnancy, GDM affects 3 - 20% of pregnancies in Canada [54]. Risk factors for GDM include being ≥ 35 years of age, being from a high risk ethnicity (i.e. African, Arab, Asian, Hispanic, Indigenous, or South Asian), having a BMI ≥ 30 kg/m^2, and/or prior history of GDM [55]. Initially pregnant individuals may present with signs and symptoms including polyphagia (i.e. constant hunger; caused by variations in blood glucose and insulin levels acting on appetite regulation [56,57]). GDM is usually diagnosed around 24 - 28 weeks of pregnancy with an oral glucose tolerance test [58] and is characterized as abnormally high plasma glucose (i.e. positive oral glucose tolerance test values: fasting ≥ 5.3 mmol/L, one hour ≥ 10.6 mmol/L, or two hour ≥ 9.0 mmol/L) [55]. Compared to a non-diabetic normoglycemic pregnancy, individuals with GDM have significantly less insulin secretion [41,59] (i.e. up to 50% less [44,45]) as well as a 30 – 40% decrease in insulin receptor tyrosine kinase activity in the skeletal muscle [60]. This means that individuals with GDM will be more likely to experience hyperglycemia (i.e. maternal glucose ≥ 11.1 mmol/L two hour post oral glucose tolerance test) which can be managed with insulin, exercise, and/or diet [58]. During pregnancy, individuals with GDM are at a higher risk of developing gestational hypertension and preeclampsia which can negatively affect fetal health and result in preterm birth [61–63]. Babies born to individuals with GDM are at an increased risk for fetal macrosomia (i.e. > 4000 g), thus increasing maternal risk for cesarian sections and fetal risk for neonatal hypoglycemia [64]. After pregnancy, individuals are also at a heightened risk of developing type two diabetes, hypertension, and cardiovascular disease within 15 years following delivery [65,66]. Thus, prevention of GDM is critical for the health of two generations.

Cardiovascular System

The cardiovascular system exhibits some of the most rapid and profound adaptations during pregnancy. One of the earliest changes is a rapid decline in maternal systemic vascular resistance which reaches its lowest point by mid-pregnancy. To counteract this adaptation, the renin-angiotensin-aldosterone system (RAAS) produces anti-diuretic hormones which cause fluid retention and blood volume increases by approximately 50% by term [67]. The maternal heart undergoes necessary structural (i.e. dilation of the valve ring, increase in myocardial thickness and mass, and larger left arterial diameter [68]) and functional adaptations in order to accommodate these cardiovascular challenges, and maintain adequate supply of oxygen and nutrients to the fetus. Over the course of pregnancy cardiac output increases by 30 – 50% [69,70]. In early gestation, the increase in cardiac output is attributed to the rise in stroke volume (i.e. by 20 – 30% [69,71]) which is the amount of blood pumped out of the left ventricle in a single contraction and is dependent on the hearts preload and afterload [26,69]. After the second trimester, stroke volume plateaus and heart rate becomes the predominant factor increasing cardiac output [26]. In a healthy pregnancy there is a progressive increase in heart rate peaking in the third trimester 15-20 beats per minute above pre-conception values [26]. The increase in maternal heart rate is due to an increase in efferent activity of the sympathetic nervous system in combination with decreased cardiac sensitivity to parasympathetic stimulation [72]. It has been suggested that the increased sympathetic activation is due to pregnancy related changes in arterial blood pressure (i.e. decrease in total peripheral resistance and systemic vascular tone) [73] which is maintained or slightly declines until the ~ 20th week of gestation [74,75]. Most, but not all studies, suggest that that systolic blood pressure decreases 5 – 10 mmHg and diastolic blood pressure decreases by 10 – 15 mmHg by mid-gestation due to the drop in systemic vascular resistance [75–77]. Following the 20th week of gestation, blood pressure steadily rises to pre-conception levels due to the rise in blood volume [76–80]. The mechanism behind the rise in blood pressure is thought to be due two factors, the rise in plasma (i.e. 30 – 50% [81]) and red blood cell production [82]. These hemodynamic adaptations facilitate the distribution of ~ 25% of maternal cardiac output for fetal development [69,74].

Prenatal Physical Activity

General Overview

The Society of Obstetricians and Gynaecologists of Canada (SOGC)/Canadian Society for Exercise Physiology (CSEP) 2019 Canadian Guideline for Physical Activity throughout Pregnancy recommends that all females without contraindications participate in 150 minutes of moderate-intensity physical activity (i.e., 64 – 76% HR_{max}) per week to derive clinically meaningful health benefits [3]. Contraindications are medical conditions in which exercise may not be beneficial to the mother and/or fetus and can be categorized into two types, absolute and relative. Females who develop absolute contraindications to prenatal exercise should avoid moderate-intensity physical activity as the potential harms to the mother or fetus outweigh the potential health benefits; however, activities of daily living under the direction of their health care provider are encouraged. Complete cessation of physical activity (i.e. bedrest) should be avoided as it has been well documented to increase the risk of physical and psychological adverse effects [83,84]. Females who develop relative contraindications (e.g. recurrent pregnancy loss, gestational hypertension, and eating disorders [85]) are encouraged to have a discussion with their health care provider prior to continuing or beginning moderate-intensity physical activity during pregnancy. When physical activity is recommended, modifications to exercise intensity, duration and/or type of activity is encouraged over a complete cessation. Achieving the recommended 150 minutes of moderate-intensity physical activity each week has demonstrated to reduce the odds of developing major pregnancy complications by 40% (i.e. preeclampsia, gestational hypertension, gestational diabetes mellitus [5]). Maintaining a physically active pregnancy can also reduce the odds of having a newborn birth weight greater than 4,000 g (i.e. macrosomia) by 39% [7], excess gestational weight gain by 32% [4] and instrumental delivery (i.e., forceps and vacuum) by 24% [6]. Prenatal physical activity at moderate-intensities has also demonstrated no increase in risk for caesareans, prolonged labour, vaginal tears, or musculoskeletal traumas [6]. Although the health benefits of moderate-intensity physical activity are well established during pregnancy, there is a lack of recommendations regarding vigorous to near maximal intensities.

A series of systematic reviews were developed to serve as the evidence base for the SOGC/CSEP 2019 Canadian Guideline for Physical Activity throughout Pregnancy identified dose response relationships demonstrating higher intensities, durations and volumes of physical activity derived greater reductions in the odds of developing gestational diabetes, gestational hypertension, and preeclampsia [3]. However, an upper limit to this relationship was not identified due to a paucity of evidence beyond moderate-intensity levels of physical activity. Currently, only three studies (Table 1) have investigated the effects of aerobic exercise surpassing 90% HR_{max} in pregnant populations with a key focus of assessing the safety of vigorous-intensity exercise on fetal wellbeing [86–88]. To summarize, fetal bradycardia/tachycardia and abnormal maternal-fetal circulation were observed in a small subgroup of individuals (n = 15) during intense (i.e. > 90% HR_{max}), prolonged exercise [86–88]. Fetal bradycardia (< 110 beats per min) and tachycardia (> 160 beats per min) are considered abnormal responses to maternal exercise [89] and may be caused by abnormalities in maternal-fetal circulation (i.e. increased resistance to blood flow at the placenta and decreased blood flow) [86,90,91]. If an increase in resistance to blood flow is detected, oxygen transfer is less effective and the risk for fetal hypoxia is increased [92]. These findings suggest that prolonged periods of vigorous-intensity physical activity (i.e. progressive four to five-minute work intervals) and graded exercise tests exceeding 90% of maternal HR_{max} may have adverse effects on fetal well-being. It is important to investigate shorter duration work intervals to determine if a durational threshold exists and if there are added benefits to utilizing recovery intervals.

To our knowledge, only three studies have investigated the effects of HIIT during pregnancy, one in rats and two in humans [14,93]. Most recently, Anderson and colleagues examined the impact of an acute HIIT resistance circuit on fetal wellbeing (i.e. fetal heart rate and umbilical artery indices) [14]. The circuit consisted of three-rounds of six exercises performed for 20-seconds (i.e. targeting 80 – 90% of maternal HR_{max}) with 60-seconds of active recovery and two-minutes of rest between rounds [14]. In total, six-minutes of vigorous-intensity exercise was accumulated during HIIT and no adverse fetal responses were reported [14]. These findings may indicate that short burst of vigorous exercise followed by periods of active recovery are less likely to cause adverse fetal effects compared to prolonged progressive exercise. In 2016 Ong and colleagues demonstrated the impact of six 15-second self-paced higher intensity efforts repeated every three-minutes (i.e. accumulation of 1.5-minutes of work with peak intensities of 83 ± 6% HR_{max}) [16]. In comparison with 20-minutes of continuous cycling at 65% $HR_{max,}$ HIIT demonstrated minimal difference in maternal blood glucose reduction (i.e., HIIT: 1.0 ± 0.3 mmol/L versus MICT at 1.1 ± 0.2 mmol/L) [16]. These findings provide a first glimpse into maternal glucose response to aerobic HIIT and suggest that further research is needed to investigate longer duration work intervals, higher target heart rates, and extended monitoring of material glycemic response. Addressing these research gaps will provide a better understanding of maternal response to greater volumes of physical activity (i.e., intensities > 90% HR_{max}), overall tolerability to traditional forms of aerobic HIIT protocols. HIIT may also offer some protective benefits in regards to oxidative stress (i.e. oxidative damage to cells and tissues [94]) in fetal heart and liver tissues as demonstrated in rats [93]. Rat fetuses also demonstrated no indications of adverse growth rates after six-weeks of maternal participation in HIIT [93]. These findings indicate that HIIT may be well-tolerated by the fetus during pregnancy and recovery intervals may be instrumental in ensuring the safe practice of vigorous-intensity exercise during pregnancy.

Compensatory Behaviours

Prenatal physical activity levels are an essential component to an individuals total daily energy expenditure and can help contribute to a reduction in many pregnancy complications [4–7]. However, the benefits of prenatal physical activity may be counterbalanced by an overall reduction in non-exercise activity thermogenesis (NEAT). NEAT (e.g. tasks of daily living) is highly variable ranging from $\leq$ 10% of total energy expenditure in sedentary populations and $\geq$ 50% in highly active adults [95,96]. In non-pregnant populations, decreased activities of daily living have been demonstrated in response to vigorous-intensity exercise interventions [97] and recent concerns have been expressed about exacerbating perceived fatigue during pregnancy with higher exercise intensites [98]. An increase in total energy intake (e.g. high calorie foods and drinks) has also been demonstrated in response to exercise interventions [99]. Although compensatory behaviours (i.e. increase in sedentary behaviour and/or caloric intake) have been identified in investigations targeting weight-loss in overweight individuals [100] , it is important to establish that vigorous-intensity physical activity during pregnancy (i.e. HIIT) doesn't facilitate these adverse effects. Previous research in older adults [101], type 2 diabetics [102], and individuals undergoing cardiac rehabilitiation [103] have previously found that chronic HIIT interventions (i.e. 4 weeks to 1-year) did not reduce NEAT and/or result in dietary changes. These findings support that HIIT may have the potential to increase total daily engery expenditure without adverse compensatory effects. Compensatory behaviours have yet to be investigated after acute aerobic HIIT interventions in pregnant populations.

Table 1: Exeeding 90% Maternal HR_{max} in Pregnant Populations

Author and year	n; Population; Week of gestation	Protocol					Results
		Modality	WU	Workloads	Duration (min)	Maximal Intensity Achieved	
Salvesen et al., 2012 [86]	6; Olympic Athletes; (23 – 29)	Treadmill	10-min; eliciting 135 bpm	Speed increased 1km/hr with each WL. Constant incline at 6%	Each WL: 5-min with 4-min of rest between each bout.	Main bout: 60 – 90% VO_{2max}	○ Four women completed 3 WL uneventfully (i.e. highest intensity achieved was 88% HR_{max}). ○ Two individuals completed 4-5 WL reaching 92 and 97% maternal HR_{max}. • Both fetus had bradycardia (103 and 92 bpm) and high umbilical artery PI (1.67 and 1.65). Volume blood flow decreased to 37% and 42% of initial values. • Fetus recovered with cessation of maternal exercise. • One of the individuals later developed HELP syndrome at 35 weeks.
Szymanski et al., 2012 [88]	15; inactive 15; regularly active	Treadmill	5-min at 3mph, 0% grade	Constant pace of 3mph, with increasing incline every 2-minutes by 2%.	Inactive: 12.1 ± 3.6 Regularly active: 16.6 ± 3.4	Inactive: 87 ± 10.8% HR_{max} Regularly active: 87.9 ± 4.8% HR_{max}	○ Umbilical and uterine artery indices and FHR were similar among the 3 activity groups. ○ Subgroup (n = 5) of highly active participants experienced transient FHR decelerations after exercise

	15; Highly active (28 – 32)			After achieving an incline of 12%, grade was maintained and speed increased 0.2 mph every 2-minutes.	Highly Active: 22.3 ± 2.9	Highly Active: 92.1 ± 5.7% HR_{max}	and elevated umbilical and uterine artery indices • Subgroup did not differ in gestational age, treadmill time, maternal peak heart rate • FHR recovered within ~ 3-minutes with cessation of maternal exercise.
Erkkola et al., 1992 [87]	8; Non-athletic (35 – 38)	Bicycle	3-min at 60rpm; 0 kp	3-stages with stepwise increases (73 ± 27, 114 ± 29, and 161 ± 16 W)	Each stage: 4-min	Average HR_{max} at end of stage: Stage 1: 70% Stage 2: 83% Stage 3: 92%	○ Correlation between increasing maternal heart rate and decrease in S/D ratio in the uterine artery ($r = 0.58$, $N = 32$, $P < 0.01$) ○ 12% decrease in flow at the highest intensities ○ SD in the umbilical artery remained unchanged compared to baseline ○ FHR increased significantly during exercise and recovery; Fetal tachycardia

BPM: beats per minute; **FHR:** fetal heart rate; **HELP**: Haemolysis-elevated Liver Enzyme-low Platelets syndrome; **HR_{max}**: Heart Rate Maximum; **Kp**: kilopond; **Km/Hr:** kilometres per hour; **Min:** minutes; **n**: number of participants; **PI:** Pulsatility Index; **Rpm**: revolutions per minute; **VO_{2max}:** Maximal rate of oxygen consumption; **W:** watts; **WL:** workload; **WU:** Warm up.

Glucose Response to Physical Activity

Glucose uptake into the skeletal muscle is facilitated through GLUT4 transporters which are simulated by the previously described insulin-dependent pathway, as well as non-insulin stimulated glucose disposal (i.e. contraction mediated pathways) that occurs with physical activity [20]. As the skeletal muscle contracts, a number of molecules converge to stimulate 5’AMP-activated protein kinase (AMPK) which initiates the translocation of GLUT4 transporters from intracellular storage deposits to the plasma membrane and T-tubules for glucose transport [104,105]. These sequence of events are independent of the hormone insulin and promote glucose uptake during exercise [20]. Acutely, maternal exercise can rapidly induce changes in blood glucose levels. A recent meta-regression analysis demonstrated a dose-response relationship between physical activity and maternal glucose; demonstrating that greater volumes, intensity and/or duration were associated with greater declines in maternal glucose from pre-to-post exercise, however the risk of hypoglycemia remained low across investigation [15].

During physical activity the skeletal muscle experiences an increase in metabolic demands resulting in an increase in carbohydrate and fat oxidization [106,107]. The degree to which carbohydrates and fat are utilized is dependent on the intensity and duration of the activity [108]. At low-intensities and/or durations exceeding 90 – 120 minutes, the predominate source of energy is derived from lipids (i.e. free fatty acids) [109,110]. However, as the physical activity transitions to a moderate-intensity [i.e. 40-50% VO_{2max}] , approximately half the energy contribution is from carbohydrate oxidation (i.e. muscle glycogen and blood glucose) [110,111] . During pregnancy individuals will experience an increased release of triglycerides from the liver during MICT resulting in higher blood concentrations post-exercise compared to pre [112,113], thus fetal malnutrition is not a concern. Peak fat oxidization occurs at ~ 50 – 55% VO_{2max} and subsequently declines with increasing intensity [110]. During vigorous-intensity physical activity carbohydrate oxidization increases to two-thirds of the contribution due to the increased metabolic demands of the skeletal muscle [114]. Meta-analyzed data has provided low certainty of evidence demonstrating low-to-vigorous intensity physical activity has a low risk (i.e., 0 – 4%) of dropping maternal glucose to the point of hypoglycemic (< 3.3 mmol/L) [15]. Once exercise intensity exceeds 75-80% VO_{2max} muscle glycogen and blood glucose become the primary resource for skeletal muscle and fat oxidization declines to or below resting values [115]. These findings support the theory of a dose response relationship between the consumption of glucose and increasing exercise intensities. Due to the intense nature of HIIT, the body would theoretically cycle between short bouts of predominately carbohydrate oxidization during work intervals and a combination of carbohydrate and fat oxidization during lower-intensity recovery intervals. Thus it is important to monitor the maternal glucose levels during HIIT as glucose will be the primary source of energy used to perform work.

The metabolic benefits of HIIT in non-pregnant individuals are well established. In individuals with type two diabetes, an acute session of HIIT (i.e. 1:1 ratio of 60-seconds for 10 work bouts at ~90% HR_{max}) has demonstrated lower rates of hyperglycemic events and reduced postprandial hyperglycaemia over a 24-hour period [23]. The glucose lowering effects of HIIT are due to increased insulin sensitivity at the skeletal muscle and can last up to 48-hours post-exercise [116]. Over a period of two-weeks, HIIT has demonstrated a 13% reduction in 24-hour blood glucose concentration and a 369% increase in GLUT4 protein content in individuals with type two diabetes [117]. These physiological adaptations increase the effectiveness of glucose reuptake by providing the skeletal muscle with a greater concentration of glucose transporters on the surface [117,118] . Thus, HIIT has the potential to provide short- and long-term health benefits to individuals with metabolic disorders including improvements in endothelial function, fasting blood glucose, and improved A1C [119]. Although HIIT has yet to be utilized during pregnancy, it could be assumed that it may be an effective treatment option for pregnant individuals struggling to cope with glycemic control, such as with GDM. In non-diabetic pregnant individuals meta-analyzed studies have demonstrated that light to moderate-intensity physical activity reduces the odds of developing GDM up to ~40% [5]. Therefore higher volumes of physical activity, such as obtained with HIIT, may be effective in maintaining metabolic health during pregnancy.

Heart Rate Response to Physical Activity

During pregnancy maternal heart rate is most commonly used to assess exercise intensity [often in combination with ratings of perceived exertion (RPE) or other subjective measures of intensity]. Across exercise physiology literature methods for prescribing exercise intensities vary (i.e., heart rate reserve, %VO2 Reserve, %$VO2_{max}$, and %HR_{max}). For clarity, the American College of Sports Medicine (ACSM) summarized the relative equivalents of each prescription method and categorizes physical activity intensity into five categories (summarized in Table 2).

For the sake of this thesis, %HR_{max} will be referenced consisting of very light (< 57% HR_{max}), light (57 – 63% HR_{max}), moderate (64 – 76% HR_{max}), vigorous (77 – 95% HR_{max}) and near maximal to maximal (≥ 96% HR_{max}) intensities [120]. As previously mentioned, HIIT elicits hearts rates ≥ 80% HR_{max} during work intervals and intersperses them with lower-intensity recovery intervals [10]. During the recovery intervals it is important to monitor maternal heart rate for normal cardiac responses (i.e. heart rate decreasing with lower intensity bouts). Abnormal cardiac responses (e.g., failure of heart rate to slow with recovery and/or inability for heart rate to increase with increasing workloads) can serve as a possible indicator of exercise intolerance. Exercise intolerance can be multifactored and is defined as a reduced capacity to perform physical activity [121]. An individual experiencing exercise intolerance may start to demonstrate symptoms such as significant dyspnea, fatigue, light-headedness, and/or dizziness [121,122]. Signs and symptoms of exercise intolerance can serve as a termination criteria for physical activity.

Evidence demonstrates that regardless of previous fitness, maternal resting heart rate increases with advancing gestational age [123], that being said, chronic aerobic exercises has resulted in lower resting heart rates than non-exercisers (i.e. improved autonomic nervous system control) [123]. Although maternal heart rate progressively increases from early pregnancy to term, maternal heart rate is roughly equivalent to their non-pregnant values during submaximal exercise [124–126]. At maximal intensities, it has been suggested that maternal maximal heart rate decreases (i.e. ~ 4 bpm) [127] or does not change when compared to pre-conception [124,128]. A possible cause of lowered maximal heart rate is reduced cardiovascular reserve (i.e. inability to increase cardiac output) caused by the elevated resting heart rate experienced during pregnancy and/or blunted catecholamine responses during exercise [126,127,129]. Thus it is to be expected that maternal heart rate should be equivalent to the non-pregnant state during aerobic HIIT unless eliciting near maximal to maximal intensities (i.e. ≥ 96% HR_{max}) during work intervals.

Table 2: Relative Intensity Prescription Methods from ACSM

Intensity	%HRR or %VO_2R	%HR_{max}	%VO_{2max}
Very light	< 30	< 57	< 37
Light	30 - 39	57 - 63	37 - 45
Moderate	40 - 59	64 - 76	46 - 63
Vigorous/high	60 – 89	77 – 95	64 - 90
Near maximal to maximal	≥ 90	≥ 96	≥ 91

ACSM, American Colledge of Sports Medicine [120]; **HR_{max}**, maximal heart rate; **HRR**, heart rate reserve; **VO_{2max}**, maximal oxygen consumption; **VO_2R**, oxygen uptake reserve.

Mode of Exercise – HIIT

General Overview

HIIT has become increasingly popular in non-pregnant populations as a way to improve fitness in a shorter period of time compared to longer duration continuous physical activity. HIIT consists of short bursts of exercise completed at intensities ≥ 80% HR_{max} [10], which are separated by brief intervals of lower-intensity active recovery. In non-pregnant populations, chronic aerobic HIIT has demonstrated improvements in an aerobic fitness (e.g. rise in VO_{2max} [11–13]), metabolic health (e.g. greater insulin sensitivity [13]) and cardiovascular wellness (e.g. endothelial and ventricle function [11,12]). Other metabolic adaptations include the up-regulation of the oxidative and glycolytic energy systems which enhance the availability of energy in the working muscle [130–133] (e.g. increased muscle mitochondrial density/citrate synthase activity by 36% [130]). Although traditionally considered a training modality for athletic populations, HIIT has also been used safely and effectively for those with pre-existing morbidities such as: cardiovascular disease [134], multiple sclerosis [135], stroke [136], obesity [137], and type two diabetes [138]. When directly comparing HIIT and MICT of equal duration (i.e. 60-minutes/session five times per week for four months), HIIT significantly enhanced an individual's VO_{2max} ($P < 0.05$), decreased their adiposity (i.e. fat mass and visceral fat; $P < 0.05$) and lower mean blood glucose ($P < 0.05$) in individuals with type two diabetes [139]. A systematic review and meta-analysis has also demonstrated that chronic HIIT (i.e. three times per week for 12 – 16 weeks) improves vascular function, insulin sensitivity, and inflammation while further reducing the risk of cardiovascular disease [140].

It is evident that long-term adherence to physical activity can result in greater maternal health benefits therefore, it is important to consider subjective factors (i.e., perceived enjoyment and rating of perceived exertion) that could impact adherence to HIIT. A previous study utilizing interval cycling (i.e. 15-second self-paced work intervals to 180-seconds of active recovery at 65% HR_{max}) has demonstrated greater perceived enjoyment with pregnant individuals describing it as "interesting" and "challenging" compared to equal durations of MICT (i.e. 20-minutes at 65% HR_{max}) [16]. However the previously described protocol is subjected to several limitations including the utilization of a less traditional HIIT prescription (i.e. 1:12 ratio) resulting in a low overall rating of perceived exertion (i.e. "light to somewhat hard") and narrowly meeting exercise intensity criteria for HIIT (i.e. 83 ± 6% HR_{max}) [16]. Consequently, enjoyment and interest to traditional aerobic HIIT during pregnancy remains unknown. In a previously described resistance circuit participants reported high levels of enjoyment and willingness to participate on multiple occasions despite it being described as 'hard' to 'very hard' (i.e. 15-17/20 on the Borg scale) [14]. The data from these studies are important as they may indicate a growing number of females interested in participating in HIIT after conception [14,16].

Safety of HIIT

Prior to engaging in HIIT, it is important to consider an individual's pre-existing health and previous physical activity history. Self-screening questionnaires, such as the Get Active Questionnaire for Pregnancy [141] and the Health Care Provider Consultation Form for Prenatal Physical Activity [142], are important tools to identify potential risks or concerns about participating in physical activity. The ACSM recommends that individuals wanting to participate in HIIT should be exercising regularly (i.e. three to five times per week for 20 – 60 minutes of 'somewhat hard' aerobic activity for several weeks) prior to beginning a new program to established a sufficient fitness base [10]. It is also important to include an appropriate warm-up/cool-down, progress slowly and establish good exercise form to reduce the risk of musculoskeletal injury [10,143]. Modifying the intensity, duration and/or modality can optimize HIIT prescription and reduce the potential for adverse responses. HIIT has been studied extensively in non-pregnant clinical populations with reassuring assessments of safety. A retrospective study assessed the risk of a cardiovascular event during HIIT in 4,846 patients (70% males; 30% females) with coronary heart disease [144]. Researchers determined patients were at low risk of adverse event reporting 1 non—fatal cardiac complication per 23,182 hours of HIIT [144]. Other studies in patients with coronary heart disease have also reported no adverse effects or contraindications to exercise during HIIT [145,146]. Currently there are no studies evaluating the safety of HIIT during pregnancy. Rather, previously inactive and active individuals, without contraindication to exercise, have been considered to have low risk of having an adverse event in response to low-to-moderate intensity physical activity during pregnancy [147]. A review investigating prenatal physical activity reported 1.4 serious events for every 10,000-hours of exercise (i.e. threatened pre-mature labour, bleeding placental previa, miscarriage and uterine contractions) in previously uncomplicated pregnancies [147]. Less serious adverse events, including mild gestational hypertension, musculoskeletal injury, low back or pelvic girdle pain, leg cramps, nausea, fatigue, and fetal bradycardia/tachycardia, occurred more frequently at 6.8 events per 10,000-hours [147]. The evidence-based risk assessment mainly focused on prenatal physical activity ranging from 50 – 70% maternal HR_{max} (light-to-moderate-intensity) [147] and therefore are limited in commenting on the possible adverse effect at vigorous-intensities. Current prenatal physical activity guidelines suggest individuals should first consult their health care providers prior to engaging in vigorous-intensity physical activity (i.e. ~ 90% maternal HR_{max}) [3]. Further research is required to establish the safety and possible benefits or risks of HIIT during pregnancy.

Protocol Specifications

When prescribing HIIT there are multiple factors that should be considered when selecting the most appropriate protocol. Firstly, it is important to consider your participants demographics (e.g., diseases status, age, physical activity history, coordination) and mode of exercise (e.g., treadmill, track, cycle ergometer). Although there is an almost infinite number of possible HIIT prescriptions (i.e. interval durations, intensities and number of bouts), the exercise session should translated into several minutes of vigorous-intensity exercise [148]. Specifically, we are interested in choosing an effective acute aerobic HIIT prescription that will elicit changes in maternal blood glucose. Our protocol will be structured after previously published work (i.e. 10-sets of 60-second work intervals $\geq$ 90% HR_{max} interspersed with 60-seconds of lower-intensity recovery) which has demonstrated a significant difference in peak glucose concentration ($P < 0.001$) and post-prandial response ($P < 0.001$), as well as lower 24-hour average blood glucose in non-pregnant individuals with type two diabetes [23]. This prescription (i.e. 1:1 ratio for 60-seconds) has also been replicated in multiple other studies appearing to be well tolerated over extended training periods (i.e. two to three weeks) in non-pregnant individuals with type two diabetes [23,149,150], obesity [151] and healthy sedentary adults [152]. This findings support the effectiveness of the HIIT prescription in eliciting glycemic responses in acute and chronic settings, as well as the transferability to other populations. Table 3 highlights the popularity of a 1:1 60-second ratio in different clinical and healthy populations, as well as responses to varying other intensities/durations.

Currently there are no recommendations specific to pregnant females regarding aerobic HIIT protocols; however, it is our intention to choose a safest practices and modality that considers the unique physiological changes that occur during pregnancy. Firstly, we will be using the resting heart rate cut off value of 120 beats per min for pregnant individuals without contraindication to exercise [153]. Pre-exercising blood pressure will also be taken to ensure it is under the resting cuff off values (i.e. $\leq$ 140 mmHg systolic and $\leq$ 90 mmHg diastolic) [153]. There is evidence that females experience higher rates of post-exercise hypotension, as well as fainting during pregnancy [154]. As well, pregnant individuals are at an increased risk of falls due to the decreased stability as their in center of gravity transitions anteriorly as pregnancy progresses [155]. Research on populations with unstable gait have focused on utilizing upright and recumbent cycle ergometers [156–158]. Benefits of cycle ergometers include a larger base of support decreasing the risk of tripping or stumbling. It is also important to include an adequate five-minute warm-up and cool down to reduce the risk of adverse events [153]. Warming up slowly increases body temperature which improves muscular compliance reducing the risk of muscular skeletal injury [159]. During pregnancy, a warm-up is especially important as individuals are at an increased risk for instability and injuries due to the pregnancy hormone relaxin which causes ligaments around joints to become lax [160,161]. Warm-ups may also prevent ischemia, as they allow the cardiovascular system to adapt to the increasing demands of exercise [162,163]. Cool-downs are beneficial as they allow for adequate recovery of the cardiovascular system and decrease the risk of sudden drops in blood pressure [153,154,164]. Given these parameters, our chosen HIIT prescription will be appropriate for pregnant populations, effective in eliciting a glycemic response, and likely to be well tolerated by participants as previously demonstrated in Table 3.

Table 3: Summary of 1:1 Ratio Cycling HIIT Prescriptions

Author and Year	Population; sex	(n)	Acute or chronic (wks.)	HIIT Prescription				Comparison			Results from HIIT
				Reps	Interval duration (seconds)	WI Intensity	RI Intensity	Type	Intensity	Total Time (min)	
Little et al. 2011 [149]	Type 2 diabetes; n/a	8	C (2) 3x/wk.	10	60	90% HR_{max}	Rest or pedal slowly at 50 watts	n/a; pre-to-post training			↓ 24-hour average blood glucose concentration after training (7.6 ± 1 vs. 6.6 ± 0.7 mmol/L) ↓ 3-hour post-prandial glucose ↑ muscle mitochondrial capacity ↑ GLUT 4 (369%) protein content (improved glucose control via skeletal adaptions)
Hood et al. 2011 [152]	Healthy; Sedentary; M4; F3	7	C (2) 3x/wk.	10	60	80 – 90% $HR_{reserve}$	30 watts	n/a; pre-to-post training			↑ muscle oxidative capacity (35%) ↑ glucose transporter protein content (260%) ↑ insulin sensitivity by ~35% after training
Tew et al. 2019 [158]	Chrohn's; 17M; 19F	36 13 (HIIT) (12 MICT) (11 CTRL)	C (12 wk. supervised; 6 months total with follow up); 3x/wk.	10	60	90% W peak	15% W peak	MICT CTRL	35% W peak	30 / 38 min	↑ VO_{2peak}, relative to control, greater following HIIT than MICT

Winding et al. 2018[150]	Type 2 Diabetes; 19M; 13F.	29 13 (HIIT) 12 (END) 7 (CTRL)	C (11) 3x/wk.	10	60	95% W Peak	20% W peak	END CTRL	50% W peak	40	↑ VO_{2peak} vs. END ↓ whole body and android fat mass vs. CTRL. ↓ visceral fat mass ↓ HbA1c ↓ fasting glucose ↓ postprandial glucose ↓ glycaemic variability
Boyd et al., 2013 [151]	Overweight / Obese; M	19 (10 LO) (9 HI)	C (3) 3x/wk.	8-10	60	100% (HI) aerobic power	No resistance cycling at 80 rpm	Interval Cycling	70% (LO) aerobic power	60s:60s	↑ VO_{2peak} in both groups from baseline. (11.0 ± 7.4% LO vs. 27.7 ± 4.4% HI) ⇆perceived enjoyment or self-efficacy btw groups
Leggate et al., 2012 [165]	Overweight / Obese; M	12	C (2) 3x/wk.	10	240	~ 90% HR_{max}	n/a	n/a; pre-to-post training			↓ waist and hip circumference (0.052) ⇆BMI ⇆Insulin sensitivity
Fu et al., 2013 [166]	Heart Failure Patients; 29M 16F	45 (15 AIT) (15 MICT) (15 GHC)	C (12) 3x/wk.	5	180	80% $HR_{reserve}$	40% $HR_{reserve}$	MICT Or CTRL	60% $HR_{reserve}$	30 (36 with WU)	↑ VO_{2peak} compared to MICT or CRTL ↑ CO ↑ cerebral/muscular hemodynamics ↓ oxidative stress/inflammation markers associated with cardiac dysfunction

Grieco et al., 2013 [167]	Healthy, recreationally active. 29F, 19M.	45 (10 MOD) (10 VIG) (12 MAX) (7 CTRL)	C (6) n/a	5	300	(VIG): 75% $HR_{reserve}$ (MAX): 90 – 100% $HR_{reserve}$	50% $HR_{reserve}$	MOD Intervals Not Exercise (CTRL)	50% $HR_{reserve}$ N/A	65 N/A	↑ VO_{2peak} in VIG and MAX over baseline values. ⇆Insulin Sensitivity between exercise groups.
Gillen et al., 2012 [23]	Type 2 Diabetes; sedentary; n/a	7 COD	A	10	60	90% HR_{max}	Rest or pedal slowly at 50 watts	No exercise CTRL.			↓ Peak glucose Concentration ($P < 0.001$) ↓ Post-Prandial (60-120 min) ($P < 0.001$) ↓ Time spent hyperglycemic ($P = 0.04$) ↓ 24-hour average blood glucose
Thum et al., 2017 [168]	Healthy, recreationally active. 4F, 8M.	12 COD	A	8	60	85% W_{max}	25% W_{max}	MICT	45% W_{max}	20	↑ Enjoyment from HIIT (0.013) ↑ HR, RPE, BLa ($P < 0.05$)

All values expressed as mean ± standard deviation. **A**, acute; **AIT**, aerobic interval training; **BLa**, blood lactate; **BMI**, body mass index; **C**, Chronic; **CO**, cardiac output; **COD**, cross over study design; **CTRL** – no exercise; **END**, endurance training; **F**, females; **GHC**, general healthcare; **HI** – High intensity / High volume; **HIIT**, high intensity interval training; **HR**, heart rate; **HR_{max}**, heart rate maximum; **$HR_{reserve}$**, heart rate reserve; **LO** – Low intensity / Low volume; **M**, males; **Max**, maximal intensity; **MICT**, moderate-intensity continuous training; **MOD**, moderate intensity; **n**, number of participants; **n/a**, data not available; **P**, P-value; **RPE**, rating of perceived exertion; **rpm**, revolutions per minute; **VIG**, vigorous intensity; **VO_{2peak}**, Peak Oxygen Consumption; **Wk.,** week(s); **$W_{peak/max}$**, peak or maximum workload.

Chapter 3: Methods

Ethical Approval

Approval for this study was received by the Health Research Ethics Board – Biomedical Panel of the University of Alberta (Pro-00103630) and conformed to the guidelines outlined in the declaration of Helsinki. Written informed consent was obtained from all participants prior to participation.

Participant Recruitment

Between December 2020 and August 2021, 71 individuals were contacted and screened for eligibility. Of the 71 potential recruits, 34 were lost to follow-up, 11 did not meet inclusion criteria, and two refused to participate (i.e., scheduling conflicts such as vacations or moving/selling house). Therefore we recruited 24-pregnant females who were $\geq$ 18 years of age, $\geq$ 20 weeks gestation and carrying a singleton pregnancy to participate in this randomized cross-over design study. Recruitment was open Canada wide and was done through convenience sampling utilizing social media (i.e., Facebook, Twitter, Instagram), the University of Alberta's research website (www.per.ualberta.ca/exerciseandpregnancy) and recruitment posters distributed at gyms and obstetric clinics in the Edmonton area. All participants were provided with an information sheet providing details about the study, and had the opportunity to answer questions with the investigator via telephone. Individuals volunteered to participate in the study and provided written, informed consent. All participants were reminded of their rights to withdraw from the study at any point, for any reason. The PARmed-X for Pregnancy [24] and a Health History Questionnaire were completed prior to participation in the study to pre-screen participants for absolute and relative complications.

Individuals were excluded if they had an absolute contraindication to physical activity during pregnancy (Table 4) as identified by the PARmed-X for Pregnancy. Individuals with relative contraindications were reviewed on an individual basis and were to speak to their health care provider prior to engaging in the study. Females were excluded if they had pre-existing cardiovascular or respiratory disease, had a multiple pregnancy (i.e., twins, triplets, or higher), or had a metabolic disease (e.g., type one or type two diabetes, GDM) [24].

Table 4: Contraindications to Physical Activity during Pregnancy

Absolute Contraindications	Relative Contraindications
• Ruptured membranes, premature labour • Persistent second or third trimester bleeding/placenta previa • Pregnancy-induced hypertension or pre-eclampsia • Incompetent cervix • Evidence of Intrauterine growth restriction • High-order pregnancy (e.g., triplets) • Uncontrolled Type One diabetes, hypertension or thyroid disease, or other serious cardiovascular respiratory or systemic disorder	• History of spontaneous abortion or premature labour in previous pregnancies • Mild/moderate cardiovascular or respiratory disease (e.g., chronic hypertension) • Anemia or iron deficiency (Hb < 100 g/L) • Malnutrition or eating disorder (anorexia, bulimia) • Twin pregnancy after 28^{th} week • Other significant medical conditions.

Note: Reprinted from *PARmed-X for Pregnancy – Physical Activity Readiness Medical Examination* [24]

Experimental Design

This was a randomized cross-over design comparing the effects of a single bout of HIIT and MICT during pregnancy. Participants were randomized to start with one of two aerobic exercise protocols using a randomization scheme (www.sealedenvelope.com) and then completed the complementary exercise protocol.

Due to the Global COVID-19 pandemic, participants were offered two types of enrollments: online or in-person. In-person participants completed their exercise sessions in a private laboratory located on the University of Alberta campus. Online participants completed both exercise sessions in their homes while being monitored by a Clinical Exercise Physiologist (J.B.W) via video call. As a requirement of the study, all online participants were required to have access to a stationary bike.

Study Design

Following enrollment into the study participants were sent welcome packages that included a brief summary of the study, instructions on device application, and all materials required for participation. At least 24-hours prior to their first exercise session, participants were asked to apply a flash glucose monitor (Freestyle Libre Pro; Abbot Diabetes Care Inc., Alameda, CA, USA), as well as a physical activity tracker [i.e., Actigraph accelerometer (ActiGraph LLC, Pensacola, FL)] that they wore continuously for seven-days. Concurrently, a daily food log and physical activity/sleep tracking also took place.

Twelve hours prior to each exercise session, participants were asked to refrain from caffeine, alcohol and strenuous exercise. Participants were provided with a standardized energy bar (Chocolate Chip Clif bars; Clif Bar & Company, California, USA) that was ingested one-hour prior to the start of exercise. Participants would then engage in two acute bouts of exercise (i.e., one HIIT and MICT session) in random order separated by 48-hours. Acute exercise sessions were performed at approximately the same time of day for each individual. Participants continued to wear their physical activity monitors and complete their tracking sheets for at least 48-hours after the competition of the second exercise protocol. At the end of the study period, all materials were returned to the laboratory using a pre-paid envelop. Study design is highlighted in Figure 1.

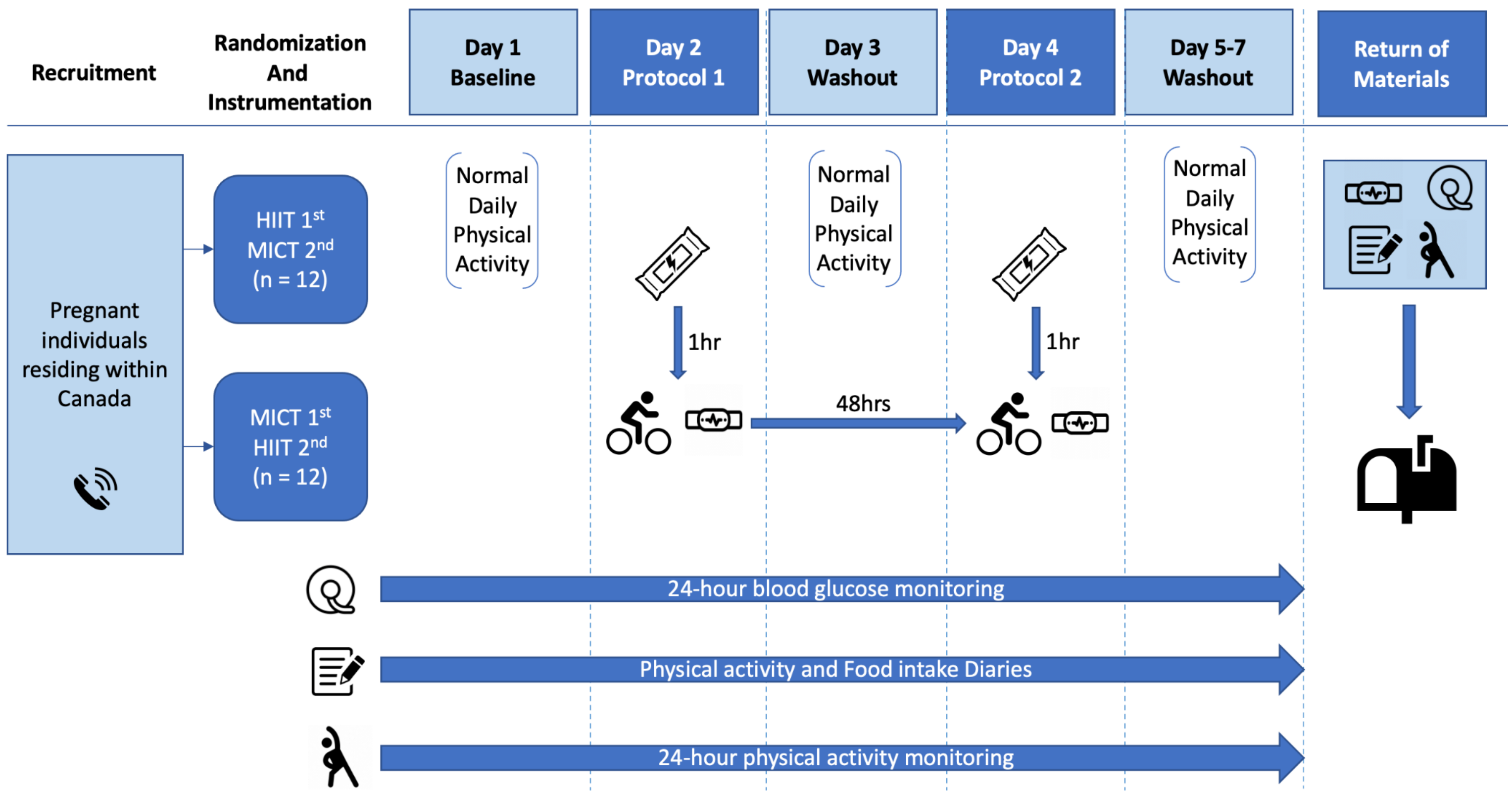

Figure 1: Study Design

HIIT, high intensity interval training; **MICT**, moderate intensity continuous training; **Hr**(s), hour(s).

: recruitment phone call; : Consumption of standardized snack; : application of heart rate monitor; : exercise intervention; : flash glucose monitor; : food and physical activity diaries; : physical activity monitor. : return of devices via mail.

Exercise Protocols

Each exercise session began with five-minutes of quiet, seated rest to obtain a stable pre-exercise heart rate. Participants began pedaling at a self-selected pace to reach a target heart rate equivalent to 57 – 63% HR_{max} (i.e., light-intensity) on a cycle ergometer for a five-minute warm up. Following the warm-up, they participated in either the HIIT or MICT protocol, followed by a five-minute cool down and finally five-minutes of quiet seated rest. The HIIT protocol, modeled after previously published work [149], consisted of 10 one-minute intervals of high-intensity work (i.e., ≥ 90% HR_{max}) interspersed with nine one-minute intervals of self-paced active recovery (19-minutes total). The MICT protocol consisted of 30-minutes of moderate intensity cycling (i.e., 64 – 76% HR_{max}). MICT and HIIT exercise protocols are summarized in figure 2.

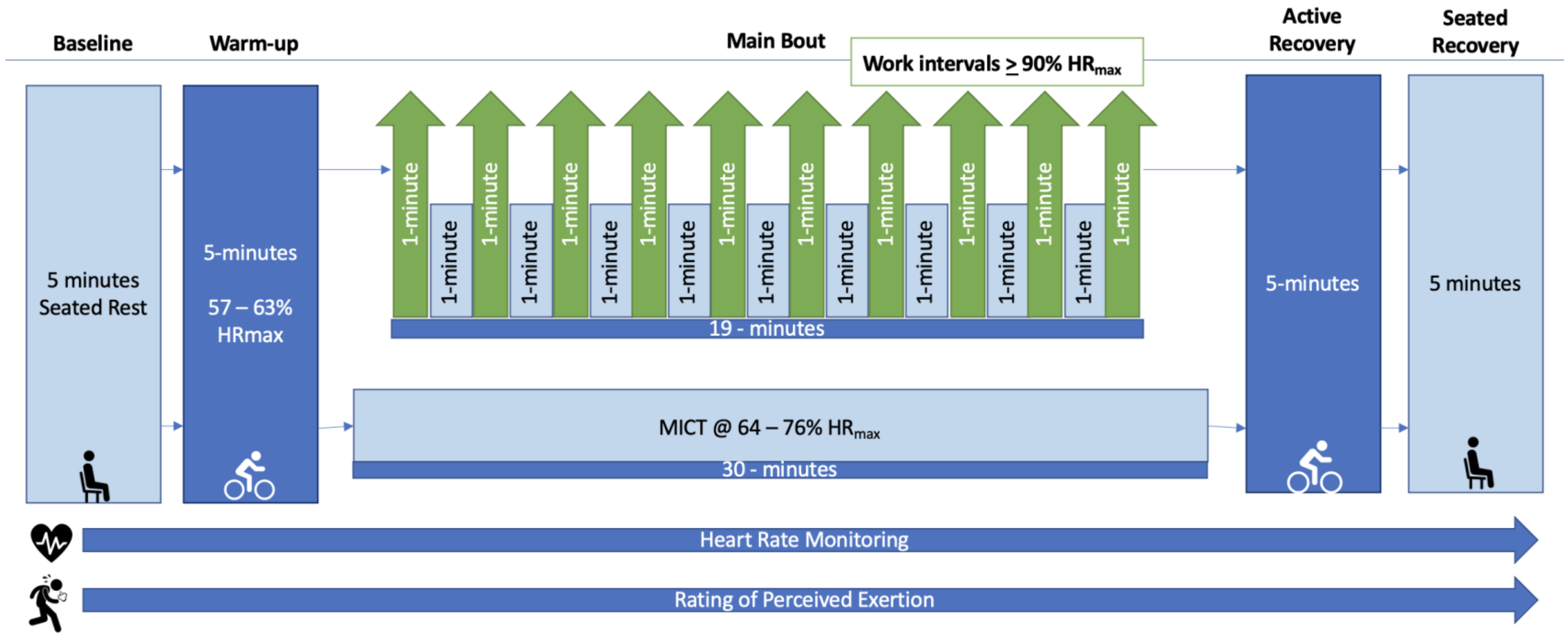

Figure 2: HIIT and MICT Exercise Protocols

HIIT, high intensity interval training; **MICT**, moderate intensity continuous training; **HR$_{max}$**, maximal heart rate.

: seated rest; : cycling on bike; : Heart rate monitoring; : rating of perceived exertion.

Study Variables / Instrumentation

Demographics: Using a standardized intake form, demographics were self-reported by participants. Demographic information included: age, height, weight, occupation, ethnicity, health information concerning pregnancy status (i.e., screening for absolute and relative contraindications) including estimated due date and current week of gestation (reported in weeks ± days), activity habits in the past month and current address. Estimated delivery date was determined using last menstrual period and later confirmed via ultrasound prior to participation.

Anthropometrics: All participants were asked to measure and self-report their height, current weight, and pre-pregnancy weight on the initial intake forms. Maternal weight was reported again during the first exercise visit. In-person participants had their measurements confirmed with a digital scale (400 Pound Physician Digital Scale; Angel, USA) and wall-mount stadiometer.

Glucose: At least 24-hours prior to the first exercise session, a flash glucose sensor (Freestyle Libre Pro; Abbot Diabetes Care Inc., Alameda, CA, USA) was inserted on to the mid-belly of the participants left tricep. For initialization, the glucose sensor was scanned twice by the handheld reader. The Freestyle Libre Pro sensor measures glucose concentrations from the interstitial fluid layer every 15-minutes [169] and has previously been used with pregnant populations to assess glycemic profile and glycemic variation during the second and third trimester [170,171]. Besides initialization, the sensor required no further participant interaction, such as scanning the device, and therefore allowed for free-living conditions and blinded subjects to their glucose values [169]. Individuals wore the sensors for seven-days, allowing for 48-hour collection periods after each exercise test. Upon sensor removal, the sensor was scanned and uploaded offline. The daily pattern and glucose pattern reports were downloaded using the Freestyle Libre Pro Software for desktop (Abbott, Chicago, IL, USA). The txt file was further analyzed using Microsoft Excel (Microsoft Software, Microsoft Corporation, Redmond, WA, USA).

Heart Rate: Predetermined heart rate zones were calculated by using the age predicted equation [(220 – age) • desired intensity] for percent HR_{max}. Prior to the exercise session, participants were fitted with a continuous heart rate monitor (Online participants: POLAR H10 Heart Rate sensor; Polar Electro, Kempele, Finland; In-person participants: EQ02+ LifeMonitor; Equivital Limited, Cambridge, UK). Online participants downloaded the Polar Beat mobile application (downloaded through the App Store or Google Play) and logged-in to the studies Polar.Flow account (flow.polar.com). Participants synced the heart rate monitors to the app which displayed their heart rate in beats per minute. Five-minutes of seated rest was recorded to determined resting heart rate. Heart rate was then monitored throughout the exercise sessions by a certified clinical exercise physiologist (J.B.W) and participants were coached to work within their prescribed heart rate zone. Heart rate was monitored during cool down, as well as five-minutes of seated recovery. After the competition of an online participant session, heart rate data was exported from Polar.Flow (Polar electro, Kempele, Finland) to Microsoft Excel (Microsoft Software, Microsoft Corporation, Redmond, WA, USA) which allowed for cleaning and second-by-second analysis. Exported heart rate data was then time matched with the recorded heart rate values collected during the session. In-person participant heart rate was continuously monitored by the same certified clinical exercise physiologist and recorded (LabChart and PowerLab; ADInstruments, Sydney, Australia). All files were later cleaned for any irregulates (e.g. heart rate outliers caused by manually adjusting the belt) and exported into Microsoft Excel for further analysis.

Interval Timer: During the HIIT and MICT exercise session an interval timer (www.intervaltimer.com) was displayed infront of participants. The timer allowed for visual feedback regarding the length of intervals, as well as overall duration of the session (i.e. warm up, main bout, and cooldown).

Rating of Perceived Exertion: RPE were reported after each work and active recovery interval during HIIT and every three-minutes during the MICT session on the 6-20 Borg scale. At the end of each exercise session, participants were asked to consider their entire session (i.e., warm up, main bout, and cool down) and report their overall session RPE on the 6-20 Borg scale.

Physical Activity and Sleep: Participants were also provided with an ActiGraph accelerometer (WGT3X-BT; ActiGraph LLC, Pensacola, FL) monitor to be worn concurrently with the glucose monitor. The ActiGraph was worn on a waist belt sitting on the right hip during waking hours and switched to a wrist strap before going to sleep. Participants kept a corresponding seven-day journal that outlined wear-time and any point in which the device was taken off for water-based activities (e.g., showering). These journals also highlighted time at which participants went to sleep, woke up, or took naps throughout the day.

Nutritional intake: Participants kept a food diary for the entirety of the study (seven-days) which detailed all meals, snacks, liquids and nutritional supplements. The time of consumption was noted for each meal and snack. When possible, weighing or measuring the food was encouraged and a visual aid was provided to help estimate food portion sizes. When cooking or baking, participants were asked to include recipes and any additional ingredients details such as brand names. Upon the study's completion, the food journals were analyzed using ESHA Food Processor ® Nutrition Analysis software Version 11.9 (ESHA Research, Salem, Oregon) for nutritional content for each day of the study. Variables of interest include mean daily caloric (kcal), fat (g), protein (g) and carbohydrate (g) intake.

Enjoyment: Enjoyment was assessed on a one-to-ten scale (1 hate, 3 unpleasurable, 5 neutral, 7 pleasant, 9 enjoyable). Once the participant had completed both MICT and HIIT sessions, they were asked to choose which session they ultimately preferred.

Standardized Snack: Participants were given two energy bars (i.e., Chocolate Chip Clif bars; Clif Bar & Company, California, USA). Participants were instructed to consume one energy bar one-hour prior to their scheduled exercise appointments.

Questionnaires

All questionnaires will be available via REDCap, a secure online website. Participants were asked to fill in a set of questionnaires:

(1) *Health History Questionnaire.* Participants were asked about their medical history, as well as information about their maternal and paternal families (i.e., anyone related by blood to the fetus). The questionnaire also asked about physical activity habits, weight changes, and diet before and during pregnancy. It also inquired about previous pregnancies (e.g., complications, weight gain, and fetal anthropometry).

(2) *Pittsburg Sleep Quality Index* (PSQI) is a self-reported questionnaire that evaluates sleep duration, latency, and other subjective means of sleep quality over a one-month period [172]. Global scores can range from 0-21, with higher scores indicating a poorer sleep quality. These components are scored and help to distinguish between "good" (PSQI score < five) and "bad" (PSQI score $\geq$ five) sleepers [173]. The PSQI has been validated for use in pregnancy [174].

(3) *Post-partum and delivery Questionnaire* inquiries about any complications that may have developed during their pregnancy (i.e., gestational diabetes, gestational hypertension, preeclampsia, prenatal depression, premature rupture of membranes, short cervix, threatened preterm labour, preterm labour, urinary incontinence, pregnancy-related low-back pain, pelvic girdle pain, or other) and maternal weight prior to giving birth. It also requested information about delivery date, gestational age at delivery, method of delivery (i.e., vaginal, planned cesarean, emergency cesarean, or instrumental), length of labour, vaginal tearing, as well as information about the baby (e.g., sex, birthweight, length, and admission to the neonatal intensive care unit).

Data Handling and Record-Keeping

Each individual participating in the study was given a study identification code in which all of our measures were associated with. All identifiable information, such as name, date of birth, and contact information is kept in personal file folders stored in a locked cabinet within a secure room. Along with individual information, a master-sheet linking identification codes to participants is stored in the same area. All members of the research team went through confidentiality training and kept all information private.

Chapter 4: Analysis

Statistical Analysis

Sample Size

Sample size was calculated based off of a previous study examining the effect of light intensity vs. vigorous intensity exercise on maternal pre-to-post-exercise glucose in females at low risk for GDM [175]. Using G*Power 3.1 statistical power analysis program [176], total sample size was set at a desired power of 0.8, cut-off for statistical significance of 0.05, and a calculated effect size of 0.8 (i.e., large). Based off of this information the estimated sample size required 15 participants. Considering the risk of drop-out, we aimed to recruit 24 females for our cross-over design. These calculations are found in Appendix E.

Statical Methods

Descriptive statistics were calculated as mean ± standard deviation and analysis occurred using statistical software (GraphPad PRISM 9 Software, San Diego, California, USA). Paired parametric t-tests were used to determine statistical differences for maternal heart rate, as well as the glucose response to acute exercise and 24-and-48-hour recovery periods. Wilcoxon matched-pairs signed rank test was used for non-parametric data, including rating of perceived exertion and enjoyment. Fisher's exact test was used to determine the influence of prior engagement of HIIT on physical activity levels. McNemar's test for matched pairs was used to determine the difference in the rate of post-exercise hypoglycemia between HIIT and MICT. Due to two participants flash glucose monitor sensors falling off early (resulting in less than 24-hours of data collection after their second exercise session), a two-way repeated measures ANOVA mixed-effect was used to take into account any missing values during the hypoglycemic, hyperglycemic and fasting glucose analysis. A two-way repeated measures ANOVA mixed effects was also utilized with nutritional intake, sleep and physical activity. For sleep analysis, a post-hoc test (i.e. Holm-Sidak) was used to identify where time points were significantly different. Raw data showing means and SD are presented in the tables or figures. Results were considered statistically significant if p-value was < 0.05.

Data Analysis

Glucose Outcomes

Interstitial glucose was used as a proxy for blood glucose and collected with the flash glucose monitor which was then downloaded with the FreeStyle Libre Software Version 1.0 software and imported to Microsoft Excel (Microsoft Software, Microsoft Corporation, Redmond, WA, USA) to be analyzed. Data inspection included time matching glucose data to detailed food intake journals and exercise test periods. A primary outcome included comparing pre- to post-exercise glucose values in both the HIIT and MICT conditions. Pre-exercise glucose was taken just prior to warm-up and compared to post-exercise glucose values recorded immediately after the main bout. To determine the effect of exercise on mean interstitial fluid glucose concentrations, we also analyzed 24 and 48-hour periods in relation to the MICT and HIIT protocols. These time blocks began at the time point at which participants consumed their standardized pre-exercise energy bar (i.e., 60-minutes prior to their scheduled assessments). Percent time spent hypoglycemic (< 3.3. mmol/L [15]) during the same 24 and 48-hour periods was also reported as a primary outcome. Abbott, the creators of Freestyle Libre, reported that Freestyle Libre Pro may inaccurately report hypoglycemic events (i.e., 40% of reports under 3.3 mmol/L, users were actually between ~ 4.4 – 8.9 mmol/L) [177]; Therefore hypoglycemic trends were considered (i.e., percent time spent hypoglycemic) rather than total number of glycemic events as per Abbott's recommendations [177]. Hyperglycemia was also represented as percent time in align with previous studies using continuous glucose monitors [23].

For fasting glucose data, the values were recorded as glucose readings taken prior to the self-reported awakening time verified by ActiGraph accelerometers. Three different mornings were taken into account per exercise protocol: the morning of the exercise testing day, the morning after the exercise protocol and the subsequent morning. Participant values were averaged and contributed to group mean and standard deviation.

Maternal Heart Rate and Rating of Perceived Exertion

Maternal heart rate was used to determine if participants were able to achieve the targeted heart rate zones set by each exercise protocol. Predetermined heart rate zones were calculated by using the age predicted equation [(220 – age) • desired intensity] for percent HR_{max}. Mean resting heart rate was determined over a five-minute period during seated rest prior to starting exercise.

Maximum/peak heart rate was determined as the highest point achieved during the main bout of the protocol and was translated into percent HR_{max}. Average heart rate took into account the entirety of the main bout as outlined in Figure 2.

One participants heart rate monitor failed to upload onto the Polar.Flow website after a HIIT session. Due to technological error, beat by beat analysis was not possible. However, during the session participant heart rate was recorded manually every 30 – 60-seconds during the protocol and therefore substituted in for analysis.

RPE was reported throughout each of the MICT and HIIT sessions. Participants also reported one overall session RPE (i.e. considering warm-up, the main bout, and cool-down). Values were averaged and contributed to the groups mean and standard deviations for each exercise protocol.

Physical Activity

Actigraph accelerometers were used to measure physical activity throughout the day. Accelerometers recorded accelerations over 60-second time intervals (epoch) and were used to determine duration (summed duration of accelerations) and intensity (magnitude of accelerations) of movement throughout the day [178]. Freedson bouts were used to determine intensity of activity and broken down into sedentary (< 100 counts per minute [cpm]), light (100 – 1951 cpm) and MVPA ($\geq$ 1952 cpm) [179]. Accelerometers also reported wear time which was confirmed using self-reported physical activity logs. Participant values were averaged and contributed to the groups mean and standard deviation. Days with < 600-minutes of wear time were excluded from analysis. One participant did not wear the Actigraph accelerometer during the study and therefore their physical activity data could not be determined. The impact of HIIT on an individual's physical activity levels was assessed by considering four different time points: the day prior to the exercise test (i.e., control), day of HIIT, and the following two days. These exact time points were also analyzed in regards to MICT to determine if participation in the exercise sessions effected their average physical activity levels.

Sleep Outcomes

Self-reported sleep logs determined sleep times in which a Cole-Kripke algorithm was used to analyze the Actigraph data. Sleep data was broken down five ways: total sleep time accumulated during the night, length of naps (i.e., occurred at least 45-minutes after reported awakening and lasted ≥ 20-minutes) combined total sleep time (i.e., sleep during the night and naps), time awake after sleep onset (WASO) and number of awakening (i.e. subject woke up for a duration of 60-seconds or more after initial sleep onset) [180]. To compare HIIT and MICT, total sleep time accumulated during the night and quality of sleep indices were pulled from the night leading up to the exercise test (i.e., protocol day) and the two nights immediately after completing the protocol.

Nutritional Intake

Participant's food journals were analyzed using ESHA Food Processor ® Nutrition Analysis software version 11.9 for nutritional content including: mean daily caloric (kcal), protein (g), fat (g), and carbohydrate (g) intake. The average daily intake was determined by analyzing all seven-days of the food diary. Furthermore, to determine the effect of caloric intake on our intervention, nutrition was analyzed over three time points: the standard 24 and 48-hour glucose periods [i.e., beginning at the time point at which participants consumed their standardized pre-exercise energy bar (60-minutes prior to their scheduled assessments)] as well as 24-hours prior to the first glucose period. Participants values were averaged and contributed to the group mean and standard deviation.

Enjoyment

Participants enjoyment was assessed using a 1 – 10 scale and overall preference for either HIIT or MICT was reported. Values were averaged and contributed to the groups mean and standard deviations for each exercise protocol.

Delivery and Fetal Outcomes

Data from the *Post-partum and delivery Questionnaire* was used to determine pregnancy and fetal outcomes. Participant values for each outcome were averaged and contributed to the groups mean.

Chapter 5: Results

Participant Demographics

Twenty-four pregnant individuals ranging from 21 – 37 weeks of gestation volunteered to participate in this randomized cross-over design study. Online enrollment accounted for 50% of participants, while the other 50% occurred in-person. Six months prior to their current pregnancy 83% of participants were partaking in either aerobic and/or resistance training HIIT and 71% continued after conception. All participants identified as women; other demographics are summarized in table 5.

Table 5: Participant Demographics

	Participants (n = 24)
Age (years)	31.5 ± 4.1
Ethnicity; n (%)	
• White / Caucasian	18 (75)
• Asian / Pacific Islander	4 (16.7)
• East Indian	1 (4.2)
• First Nations, Metis, Inuit, or Alaska Native	1 (4.2)
Highest level of Education; n (%)	
• High School	1 (4.2)
• College	2 (8.3)
• University:	
○ Bachelor	13 (54.2)
○ Masters	6 (25)
○ Doctorate	2 (8.3)
Pre-pregnancy Body Mass (kg)	70.0 ± 11.3
Pre-pregnancy BMI; n (%)	25.2 ± 4.2
• Underweight (< 18.5)	0 (0)
• Normal (18.5 – 24.9)	15 (62.5)
• Overweight (25 – 29.9)	6 (25)
• Obese (≥ 30)	3 (12.5)
Body Mass at time of participation (kg)	79.4 ± 11.6
Gestational Age at time of participation (weeks)	27.8 ± 4.7

Unless otherwise indicated, values are expressed as mean ± standard deviation. **n**, number of individuals; **%**, percentage of total participants. **BMI**, body mass index. **HIIT**, high intensity interval training. **MICT**, moderate intensity continuous training.

HIIT and MICT Exercise Sessions

All participants completed an acute bout of HIIT and MICT in random order. Exercise sessions utilized the same cycle ergometer for both sessions and started at a similar time of day. Minor symptoms including transient light-headedness ($n = 2$) and muscle cramps ($n = 1$) were reported during the acute HIIT session. One participant reported having pelvic girdle pain following their MICT session. No other adverse maternal or fetal outcomes were reported during or following the HIIT or MICT sessions.

Maternal Heart Rate and Rating of Perceived Exertion

Maternal heart rate at rest was not different between the HIIT and MICT sessions (see Table 6). As expected, average maternal heart rate throughout HIIT (82 ± 4% HR_{max}) was higher than MICT (74 ± 4% HR_{max}; < 0.0001). All participants had a peak heart rates ≥ 85% HR_{max} during the HIIT session with 18 individuals achieving intensities ≥ 90% HR_{max}. All participants achieved an average heart rate of at least 65% HR_{max} during the MICT session; however, eight individuals had an average heart rate in the vigorous zone (77 – 82% HR_{max}). Regardless, all participants engaged in a statistically higher intensity of exercise in the HIIT vs. MICT session. Participants also achieved a higher heart rate and RPE during the HIIT compared to the MICT session ($p < 0.01$).

Table 6: Maternal Heart Rate Response and Rating of Percieved Exertion to an Acute HIIT and MICT Session

	HIIT (n = 24)	MICT (n = 24)	P-value
Maternal Heart Rate			
Resting HR (bpm)	84 ± 12	84 ± 12	0.73
Average HR During Exercise (bpm)	155 ± 8	140 ± 8	**< 0.0001**
Peak HR achieved (bpm)	174 ± 7	152 ± 9	**< 0.0001**
*Peak HR Achieved (bpm)	159 – 185	136 - 173	**---**
Relative Intensity			
Average HR during Main Bout (%HR_{max})	82 ± 4	74 ± 4	**< 0.0001**
Average HR during WI (%HR_{max})	83 ± 4	---	---
Average HR during RI (%HR_{max})	81 ± 4	---	---
Peak HR achieved (%HR_{max})	92 ± 3	81 ± 4	**< 0.0001**
*Peak HR achieved (%HR_{max})	85 – 97	71 - 88	---
Rating of Perceived Exertion			
Average RPE	15 ± 1	12 ± 2	**< 0.0001**
Max RPE Achieved	18 ± 1	13 ± 2	**< 0.0001**
§ Overall Session RPE	16 ± 2	12 ± 2	**< 0.0001**

Unless otherwise indicated, values are expressed as mean ± standard deviation. A paired parametric t-test was used to determine statistical difference between groups for maternal heart rate. A Wilcoxon matched-pairs signed rank test was used to determine statistical difference between groups for rating of perceived exertion. Significant values were bolded where appropriate. ***** = indicates values are expressed as a range; **Bpm**, beats per minute; **HIIT**, high intensity interval training; **HR,** heart rate; %**HR_{max},** percentage of maximum heart rate achieved; **MICT**, moderate intensity continuous training; **n**, number of individuals; **RI,** recovery interval; **RPE**, rating of perceived exertion; **WI**, work interval §, indicates a n = 22 for HIIT and MICT.

Glucose

Interstitial glucose values were not different between HIIT or MICT pre- or post-exercise. Immediately following HIIT, fewer individuals experienced post-exercise hypoglycemia (< 3.3 mmol/L) compared to MICT (see Table 7). Of the eight individuals with an average heart rate in the vigorous zone during MICT, only one experienced post-exercise hypoglycemia. All remaining variables were not different between groups.

Table 7: Glucose in Response to Acute HIIT and MICT

	HIIT (n = 24)	**MICT (n = 24)**	**P-value**
Acute Exercise			
Pre-Exercise Glucose (mmol/L)	4.76 ± 0.98	4.80 ± 0.88	0.81
Post-Exercise Glucose (mmol/L)	4.15 ± 0.62	3.98 ± 0.98	0.32
Change in glucose Pre-to-Post Exercise (mmol/L)	0.62 ± 1.00	0.81 ± 1.05	0.30
§ Post-Exercise hypoglycemia; n (%)	2 (8)	8 (33)	**0.04**
Recovery			
Mean 24-hour glucose (mmol/L)	4.30 ± 0.44	4.34 ± 0.43	0.48
Mean 48-hour glucose (mmol/L)	4.38 ± 0.40	4.35 ± 0.4	0.47
† **Time Spent < 3.3mmol/L**			0.14
24-hour (%)	10.37 ± 13.50	8.81 ± 11.79	
48-hour (%)	6.97 ± 11.32	7.25 ± 9.29	
† **Time Spent $\geq$ 7.8 mmol/L**			0.20
24-hour (%)	0.22 ± 0.53	0.35 ± 0.96	
48-hour (%)	0.00 ± 0.00	0.36 ± 1.32	
† **Fasting Glucose**			0.86
Pre-exercise Morning (mmol/L)	3.55 ± 0.80	3.53 ± 0.65	
Post-Exercise Morning 1 (mmol/L)	3.70 ± 0.57	3.70 ± 0.63	
Post-Exercise Morning 2 (mmol/L)	3.75 ± 0.62	3.70 ± 0.52	

Data retrieved from flash glucose monitor. All values are expressed as mean ± standard deviation. A paired parametric t-test was used to determine statistical difference between groups for acute exercise and recovery unless otherwise indicated. A McNemar's test (indicated by §) or two-way repeated measures ANOVA (indicated by †) was used to determine statistical difference between groups. Significant values were bolded where appropriate. **HIIT**, high intensity interval training; **MICT**, moderate intensity continuous training; **n (%)**, number of individuals and percentage of total participants.

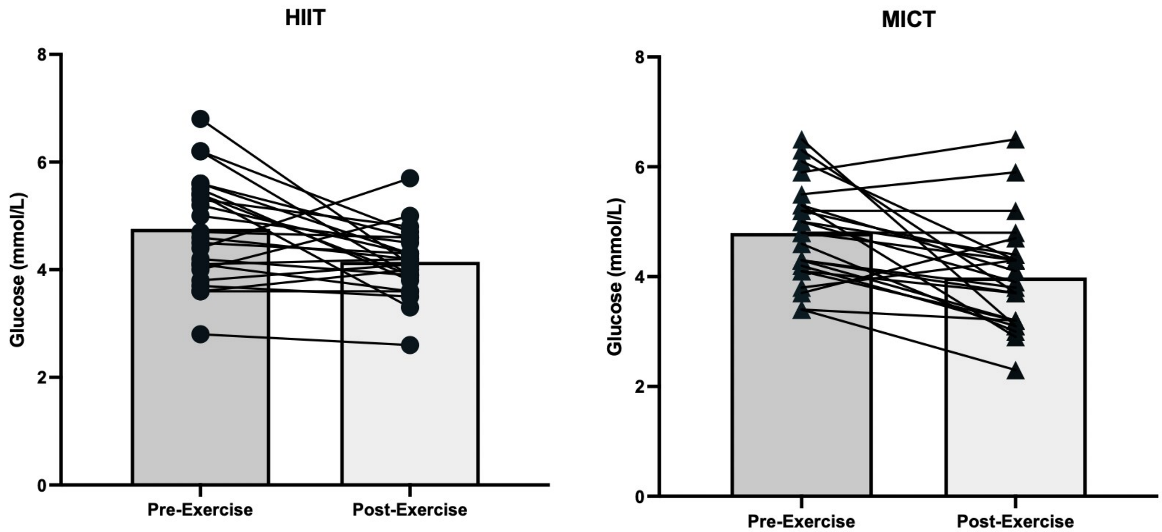

Figure 3: Change in Maternal Glucose from Pre to Post Exercise During HIIT and MICT Exercise Session

Change in HIIT from pre to post exercise was 0.62 ± 1.00 mmol/L compared to MICT at 0.81 ± 1.05 mmol/L.

Sleep

Overall, subjective rating of sleep quality using the PSQI survey classified 70% of participants as 'bad' sleepers. On average, participants slept 423 ± 17 minutes per night (7 ± 0.2 hours). Sleep duration (i.e. at night, naps, and combined; Table 8) demonstrated a significant effect over time. Post-hoc mixed effect for multiple comparisons (Holm-Siadk) revealed longer duration sleep following exercise compared to the night before the session [main effect for time points for HIIT: 52 ± 73 minutes (P = 0.0028); but not MICT [12 ± 63 minutes (P = 0.84)]. An interaction effect was demonstrated between the number of awakenings (P = 0.012) and total wake time after the onset of sleep (P = 0.032). Post-hoc mixed effect also indicated a greater number of awakenings after engaging in HIIT compared to the day following (main effect for time points: Δ5 ± 10 more awakenings night of HIIT; P = 0.019).

Table 8: Sleep Prior to and After Participating in HIIT and MICT

Sleep	HIIT (n = 23)			MICT (n = 23)			P-value	P-value	P-value
	Prior to	***Night of***	***Following***	***Prior to***	***Night of***	***Following***	**(Exercise)**	**(Time Points)**	**(Interaction)**
At Night (min)	398 ± 70	451 ± 68	412 ± 84	419 ± 66	431 ± 61	422 ± 77	0.842	**0.017**	0.157
Naps (min)	1 ± 7	11 ± 29	28 ± 44	3 ± 11	16 ± 38	6 ± 14	0.321	**0.038**	0.052
CS (min)	400 ± 68	462 ± 64	440 ± 88	422 ± 64	446 ± 61	428 ± 75	0.779	**< 0.001**	0.144
WASO (min)	66 ± 35	72 ± 41	61 ± 45	60 ± 37	58 ± 38	72 ± 42	0.473	0.762	**0.032**
Awakenings (#)	17 ± 9	19 ± 11	14 ± 8	16 ± 8	15 ± 8	17 ± 10	0.337	0.684	**0.012**

Data derived from Actigraph. All values are expressed as mean ± standard deviation. Two-way repeated measures ANOVA mixed effect was used to determine statistical difference between groups. Significant values were bolded where appropriate. **CS**, Combined Sleep (i.e., sleep at night and naps); **HIIT**, high intensity interval training. **MICT**, moderate intensity continuous training; **Min**, minutes; **n**, number of individuals; **WASO**, wake after sleep onset; **#,** number of awakenings after onset of sleep.

Rating of Perceived Enjoyment

When participants were asked if they preferred the acute HIIT or MICT session, 87.5% voted for HIIT. Perceived enjoyment of the exercise sessions was significantly different between HIIT and MICT (table 9), indicating greater enjoyment from aerobic HIIT. Enjoyment scale is located in Appendix F.

Table 9: Rating of Percieved Enjoyment in Relation to HIIT and MICT

	HIIT (n = 24)	**MICT (n = 24)**	**P-value**
Overall Enjoyment	7.75 ± 1.51	6.58 ± 1.98	**0.015**

All values expressed as mean ± standard deviation. A Wilcoxon matched-pairs signed rank test was used to determine statistical difference between groups. Significant values were bolded where appropriate. **HIIT**, high-intensity interval training; **MICT**, moderate-intensity continuous training; **n**, number of individuals.

Overall Nutrition and Physical Activity

On average, participants ate 2583 ± 463 kcal per day. Nutritional intake was not different between MICT or HIIT sessions, or during the 24- and 48-hours periods (Table 10). On average participants spent approximately 67.06 ± 7.62% of their day sedentary, 29.89 ± 6.67% participating in light physical activity, and only 3.06 ± 1.82% achieving MVPA. Minutes per day of sedentary behaviour, light and MVPA did not differ between HIIT and MICT (Table 11). Of the 22 participants who wore their Actigraph accelerometers, 16-individuals met the 150-minute of moderate-intensity physical activity per week prescribed by the 2019 Canadian Guidelines for Physical Activity Throughout Pregnancy [3]. Participants that had previously engaged in HIIT prior to or during their current pregnancy had a greater likelihood of achieving 150-minutes of moderate-intensity physical activity each week ($P = 0.046$ and 0.004, respectively) compared to those with no HIIT experience.

Table 10: Caloric Intake in Regards to Acute HIIT and MICT Sessions

	HIIT (n = 24)			**MICT (n = 24)**			**P-value**	**P-value**	**P-value**
	Prior	***24-hrs***	***48-hrs***	***Prior***	***24-hrs***	***48-hrs***	**(Exercise)**	**(Time)**	**(Interaction)**
Calories (kcal)	2596 ± 876	2745 ± 1023	2772 ± 795	2441 ± 759	2448 ± 733	2575 ± 666	0.10	0.63	0.90
Protein (g)	112 ± 37	109 ± 40	112 ± 45	100 ± 39	100 ± 39	102 ± 38	0.11	0.92	0.99
Carbs (g)	316 ± 120	338 ± 133	323 ± 113	314 ± 128	300 ± 71	308 ± 63	0.31	0.98	0.71
Fat (g)	101 ± 45	114 ± 71	119 ± 52	96 ± 40	100 ± 47	107 ± 39	0.17	0.32	0.91

Data retrieved from food diaries. All values are expressed as mean ± standard deviation. A two-way repeated measures ANOVA mixed methods effect were used to determine statistical difference between groups. **Carbs**, carbohydrates; **g**, grams; **HIIT**, high intensity interval training; **hrs**, hours; **kcal**, kilocalories; **MICT**, moderate intensity continuous training; **n**, number of participants.

Table 11: Physical Activity Intensity Prior to and Following Exercise Intervention

Physical Activity	HIIT (n = 22)				MICT (n = 22)				P-value (Exercise)	P-value (Time)	P-value (Interaction)
	Day Prior	*Day of*	*Post -1*	*Post - 2*	*Day Prior*	*Day of*	*Post -1*	*Post - 2*			
Sedentary (min/day)	578 ± 165	611 ± 141	617 ± 166	596 ± 23	552 ± 168	610 ± 129	569 ± 157	548 ± 167	0.13	0.10	0.45
Light (min/day)	263 ± 102	251 ± 68	232 ± 64	263 ± 99	241 ± 63	260 ± 68	270 ± 96	275 ± 85	0.45	0.32	0.07
MVPA (min/day)	27 ± 20	21 ± 15	26 ± 24	25 ± 23	31 ± 26	31 ± 26	34 ± 30	21 ± 14	0.26	0.27	0.36

Data derived from Actigraph accelerometer All values are expressed as mean ± standard deviation. Two-way repeated measures ANOVA mixed effect was used to determine statistical difference between groups. **HIIT**, high intensity interval training; **MICT**, moderate intensity continuous training; **MVPA**, moderate-to-vigorous physical activity.

Pregnancy Complication and Delivery Outcomes

To date, all of the study's participants have given birth, only 3 individuals did not respond to follow-up. Notably, ~ 24% of participants have developed a form of gestational hypertension. The prevalence of other complications developed during pregnancy have been summarized in table 12. On average, participants delivered at 39 ± 1 weeks of gestation. Cesarians were performed ~ 43% of the time. Of the 47.6% that delivered vaginally, 80% experienced vaginal tearing and/or episiotomy. Three infants were born with fetal macrosomia, two born vaginally (with one individual experiencing grade two vaginal tearing) and the other delivered via cesarean. Only one baby was born with complications resulting admission to the NICU, all other babies delivered were born healthy. Delivery outcomes are summarized in table 13.

Table 12: Prevalence of Pregnancy Complications

Complications; n (%)	**Prevalence (n = 21)**
Pregnancy-related low-back pain	12 (57)
Pelvic Girdle Pain	10 (47.6)
Urinary incontinence	4 (19)
Pre-eclampsia	3 (14.3)
Gestational hypertension	2 (9.5)
Pre-natal depression	1 (4.8)
Gestational Diabetes Mellitus	0 (0)
Pre-mature rupture of membranes	0 (0)
Short cervix	0 (0)

All values are expressed as the number of individuals (n) and the corresponding percentage of participants. **n**, number of individuals; **%**, percentage of total participants.

Table 13: Delivery Complications

	Delivery Outcomes (n = 21)
Gestational Age (wks.)	39 ± 1.20
• Preterm Birth (< 37 wks); n (%)	0 (0)
Maternal Weight Prior to Delivery (kg)	84.15 ± 11.75
Delivery Method; n (%)	
• Vaginal	10 (47.6)
• Cesarean (planned)	6 (28.6)
• Cesarean (emergency)	3 (14.3)
• Instrumental (i.e., forceps)	2 (9.5)
Duration of Labor (hrs)	12.28 ± 12.87
Vaginal Tears; n (%)	8 (38.1)
• 1^{st} Degree; n	2
• 2^{nd} Degree; n	5
• Episiotomy; n	1
Fetal Birth Weight (g)	3423 ± 416
• Microsomia (< 2500g); n (%)	1 (5)
• Normal (2500 – 4000 g); n (%)	17 (81)
• Macrosomia (> 4000 g); n (%)	3 (14)
Fetal Length (cm)	50.53 ± 2.60
Fetal Sex; n (%)	
• Females	13 (62)
• Males	8 (38)
NICU; n (%)	1 (4.8)

Unless otherwise indicated, values are expressed as mean ± standard deviation. **Hrs**, hours; **Kg,** kilograms; **n**, number of individuals; **NICU**, newborn intensive care unit; **Wks**, weeks; **%**, percentage of total participants.

Chapter 6: Discussion

The present study compared the effects of an acute bout of HIIT versus MICT on maternal glucose concentration in 24-pregnant participants. Overall, we demonstrated no difference in the glucose response to an acute bout of exercise (i.e. pre-to-post exercise, as well as the 24-hour and 48-hour responses) between conditions with the exception that fewer participants experienced post-exercise hypoglycemia following HIIT compared to MICT. Whereas previous HIIT studies have demonstrated peak maternal heart rates between 80 – 90% HR_{max} [14,16], 75% of our participants were able to achieve the target heart rate goal of ≥ 90% maternal HR_{max} with the highest achieved maternal heart rate equating to 97% HR_{max}. No adverse effects after participation in HIIT were reported. Physical activity and caloric intake did not differ between days or conditions; however, participants experienced prolonged sleep duration after participating in HIIT along with an increased number of nightly awaking's. Finally, despite greater ratings of perceived exertion from the HIIT session, participants in our study indicated that they experienced higher levels of perceived enjoyment during HIIT compared to MICT. Our findings contribute important insights into the impact of acute HIIT on maternal glycemic response and provide evidence of aerobic HIIT being well-tolerated during pregnancy.

Post-Exercise Hypoglycemia

The glucose-lowering effects of maternal exercise are well established. Data from a recent systematic review and meta-analysis demonstrate an average 0.6 mmol/L reduction in maternal capillary glucose in response to an acute bout of light-to-vigorous intensity exercise with relatively low risk (0 – 4%) of inducing hypoglycemia [15]. The meta-regression analysis also indicated a dose-response relationship between exercise intensity/duration and maternal glucose consumption [15]. In the current study the standardized exercise sessions were based on commonly used MICT and HIIT protocols. [23,117,150,152,158,181,182]. However, the exercise protocols were not matched for the volume of physical activity as it was greater for MICT (i.e., 64 – 76% HR_{max} for 30-minutes; 240 MET-minutes per session) compared to HIIT (i.e., 10-minutes of ≥ 90% HR_{max} with nine-minutes of self-paced recovery; 153 MET-minutes per session). Assuming a dose response relationship, the greater volume of physical activity would account for a larger decline in maternal glucose and increase rates of post-exercise hypoglycemia demonstrated within our MICT condition compared to HIIT.

Despite up to 33% of participants experiencing post-exercise hypoglycemia, they were not symptomatic (e.g., experiencing dizziness or lightheadedness) after participating in MICT or HIIT. The rate of hypoglycemic events reported within the present study should be interpreted with caution as low glucose values may be a result of inaccurate glucose sensor readings. In a clinical study, the Freestyle Libre Pro was compared to fingerstick capillary and venous blood glucose samples revealing that glucose readings below 3.3 mmol/L were inaccurate up to 40% of the time [177]. This is common among commercially available glucose monitors with lowest sensor accuracy occurring during hypoglycemia and highest accuracy during hyperglycemia [183]. However, these devices provide a greater understanding of changes in glucose values with readings every 15-minutes compared to conventional fingerstick blood samples which are traditionally only taken pre-and-post exercise. It has also been observed that interstitial glucose values remain within close approximation of blood glucose concentrations (i.e., mean difference of 0.13 ± 0.03) with the exception of when systemic blood glucose decreases < 3.3 mmol/L [184]. During periods of hypoglycemia, interstitial glucose values decline more rapidly and reveal lower concentrations compared to blood glucose [184,185]. Although sensor accuracy may account for the high rates of post-exercise hypoglycemia, this phenomenon may be due to a blood-interstitial fluid glucose concentration gradient in which insulin acts upon the cells at the level of the tissues [184,185]. Future investigations would benefit from both flash glucose monitors and fingerstick blood samples when comparing pre-to-post exercise glucose values. Overall, it would appear that an acute session of HIIT does not appear to increase the odds of post-exercise hypoglycaemia in comparison to MICT.

Fasting Glucose

Fasting glucose can serve as an indication of the effects of prenatal exercise on maternal glycemic control [15]. It is expected that the glucose lowering effects of HIIT may increase insulin sensitivity up to 48-hours post-intervention [116] thus potentially reducing fasting glucose. As observed in non-pregnant normoglycemic populations, HIIT has been effective at lowering fasting glucose values (i.e., reduction of 0.13 mmol/L compared to baseline) following an intervention lasting at least two weeks [186]. Contrary to these findings, our study demonstrated that an acute session of HIIT did not affect maternal fasting glucose within the two mornings following participation in comparison to MICT. This may be due to the lack of training stimulus obtained with a single session of HIIT in comparison to a chronic intervention. Physiological adaptations of a normal pregnancy, including increased gluconeogenesis at the liver and increased number/size of beta cells, may also account for the body's ability to maintain maternal glucose levels of after exercise [59]. In support of this, meta-analyzed data has demonstrated that non-diabetic normoglycemic pregnant individuals have demonstrated no change in fasting glucose after chronic participation in light-to-vigorous-intensity physical activity [15]. Thus, it is reasonable to suggest that an acute HIIT session does not adversely affect fasting glucose during pregnancy in comparison to MICT.

In the present study, the average maternal fasting glucose prior to and following MICT and HIIT exercise sessions ranged from 3.50 – 3.75 mmol/L. This is slightly lower than expected, as previous reports of maternal fasting glucose values are anticipated to be ~ 4.2 mmol/L within the second and third trimester of pregnancy [17]. As previously discussed, the discrepancy of lower maternal glucose values may be a result of sensor error and/or the blood-interstitial fluid glucose concentration gradient. However, our findings may also suggest that pregnant individuals may be prone to experiencing asymptomatic nocturnal hypoglycemia. Nocturnal hypoglycemia has been previously reported in pregnant populations with type one and type two diabetes, suggesting similar time spent below 3.9 mmol/L and 2.8 mmol/L (i.e., 1.3 – 1.5 hours and 0.3 – 0.5 hours, respectively) [187]. However, the frequency of nocturnal hypoglycemia in non-diabetic pregnant populations is unclear. Two studies have demonstrated conflicting results in non-diabetic pregnant populations; with the rate of hypoglycemia reported to be 13 ± 15% throughout the day and overnight [188], whereas Yogev and colleagues reported no hypoglycemic events within three subsequent nights [189]. An alternative explanation for lower than expected maternal fasting glucose values may be due to the placement of the flash glucose sensors. When flash glucose sensors are compressed, such as when they are being slept on overnight, interstitial fluid volume is reduced and the sensors sensitivity to glucose decreases [190]. Thus future investigations would benefit from fingerstick blood samples to confirm nocturnal glycemic trends.

24- and 48-Hour Glucose

Contrary to our hypothesis, 24-and-48-hour mean maternal glucose was not different between the MICT and HIIT protocols. While our HIIT protocol previously demonstrated 24-hour reductions in mean glucose in non-pregnant type two diabetics [23], it is possible that greater volumes of HIIT are needed to observe an effect in non-diabetic normoglycemic individuals. As expected, time spent in hyperglycemia (i.e., $\geq$ 7.8 mmol/L) was similar after participating in HIIT and MICT. Although no signs or symptoms of hypoglycemia were reported after participation in HIIT and MICT, our participants spent approximately 2-to-2.5-hours < 3.3. mmol/L throughout the day and overnight within the 24-hours period. These values are not unexpected as similar percent time hypoglycemic (i.e., two-hours) has been reported in asymptomatic normoglycemic pregnant individuals in the absence of an exercise intervention [191]. However, further research utilizing capillary or blood glucose values to confirm these findings are warranted.

Enjoyment

Time efficiency is one of the leading appeals of HIIT as it overcomes the primary barrier to physical activity (i.e. perceived lack of time) requiring ~ 40% less time commitment to achieve similar health benefits to MICT [21]. This may be appealing to expecting mothers as current adherence rates to the physical activity guidelines (i.e. 150-minutes of moderate-intensity physical activity per week [3]) are low (i.e. ~ 15%) [192,193]. In comparison, 73% of our participants adhered to these guidelines. Of the individuals meeting the guidelines, 93.8% had previously engaged in HIIT within 6-months prior to their current pregnancy and 87.5% participated in HIIT during pregnancy; thus, translating to a greater likelihood of achieving 150-minutes of moderate-intensity physical activity each week (P = 0.046 and 0.004, respectively). The majority of participants achieving physical activity guidelines also reported preferring HIIT (93.8%) over MICT. It is well accepted that perceived enjoyment can be a psychological motivator for increasing physical activity adherence [194] as well as an indicator of future participation [195]. However, it is important to acknowledge the potential for self-selection bias within the present findings considering the high percentage of participants with prior HIIT experience and the voluntary nature of the study. Of the four individuals with no prior experience with HIIT, 75% did not adhere to physical activity guidelines and 50% preferred MICT compared to HIIT. Thus, prior training experience with HIIT may influence overall enjoyment of the exercise session. However, aerobic and resistance circuit HIIT have been well perceived by pregnant participants with high rates of perceived enjoyment [14,16]. Anderson and colleagues reported 93% of pregnant resistance circuit participants expressed a willingness to participate again in the future [14]. Likewise, using the physical activity enjoyment scale (PACES), aerobic HIIT was determined to be significantly more enjoyable than MICT [16]. The longitudinal effect of HIIT on perceived enjoyment are still unknown within pregnant populations, however Ong and colleagues reported that when asked about a 3-month cycling program, pregnant participants expressed an greater interest in participating in HIIT (67%), or a variation of HIIT and MICT (25%), compared to MICT alone (8%) [16]. Collectively, Anderson et al., Ong et al., and our study have demonstrated the growing public interest in participating in HIIT during pregnancy despite a lack of official guidelines [14,16]. Addressing the paucity of research on the effects and safety of HIIT is crucial as public access to online HIIT workouts, blogs, advice columns, and magazine articles continue to developed despite a lack of scientific evidence [8].

Physical activity and Caloric Intake

Traditionally, the strenuous nature of vigorous-intensity exercise has led to concerns that the benefits of these activities, such as HIIT, would be counterbalanced by a reduction in overall physical activity levels outside of the exercise session due to an increase in perceived fatigue [196]. Through objective measures of free-living physical activity and self-reported dietary records we were able to examine whether an acute bout of HIIT during pregnancy resulted in compensatory behaviours. Compensatory behaviours are concerning as they may undermine the health benefits achieved through physical activity [196]. Despite the significantly greater session and exercise rating of perceived exertion during HIIT, objectively monitored physical activity patterns (i.e., sedentary, light, and moderate-to-vigorous intensity physical activity) were not different on the day prior to, of, or following HIIT compared to MICT. Although self-reported dietary recall has demonstrated significant limitations [197], particularly with pregnant individuals underestimating their daily energy intake by 45% [198], our crossover study design demonstrated no difference in energy intake (i.e., total calories, protein, fat, or carbohydrates) between days or MICT and HIIT conditions. Similar findings have been found in non-pregnant populations in which HIIT did not result in reduced daily energy expenditure [101], increased sedentary minutes [101], or dietary compensations [103]. Thus, our findings support that an acute session of aerobic HIIT does not appear to facilitate adverse lifestyle modifications during pregnancy.

Sleep

Sleep is an essential process that aids in normal physiology functioning during pregnancy. The National Sleep Foundation recommends that adults (18 – 60 years old) should sleep at least seven hours per night on a regular basis and approximately nine hours when recovering from a sleep debt or illness [199]. In the current study, participants narrowly satisfied sleep recommendations with only 6.6 – 7 hours of sleep per night. It is established up to 97% of pregnant females report disturbed sleep by the third trimester [200–203] with commonly reported reasons including physical discomforts, fetal movement, acid reflux and increased frequency of urination [200,204]. A longitudinal study reported that as pregnancy progresses, individuals experience shorter durations of sleep at night (i.e. decreasing from 7.61 to 6.85 hours per night), as well as an increase in the number and overall duration of awakenings [200]. Short sleep duration (less than six hours per night) has been associated with adverse pregnancy outcomes including prolonged labor [205], preterm delivery [206], and a 450% increase in the odds of having a cesarean delivery [205]. Optimizing sleep is critical to maternal/fetal health. Previous studies have established that low-to-moderate intensity physical activity improves sleep duration and quality in pregnant populations [207–210]. In non-pregnant populations aerobic HIIT interventions (i.e., 1 – 12 weeks) saw improved sleep quality [211–213], decreased fatigue [212], and lower cortisol levels [213].

Similar to previous findings, after engaging in HIIT our participants demonstrated an increase in sleep duration to ~ 7.5 hours (i.e., 52 ± 73 minutes longer compared to the night prior) whereas no significant change was seen with MICT (i.e., 12 ± 63 minutes longer compared to the night prior). Although not significant, in addition to accumulating a longer sleep duration, participants had reduced time spent performing light-intensity physical activity the day after HIIT (i.e., approximately 31 minutes less) compared to the day prior to and two days post-exercise. The clinical significance of this finding is unclear, while the novelty of the training stimulus may have contributed to longer sleep duration, participants also experienced the highest number awakenings after participating in HIIT. Further work is required to better understand the impact of HIIT on maternal sleep pattens.

Strengths and Limitations

Strengths of the current study include it's randomized cross-over design removing participant variability between interventions and its large sample size for data analysis. The chosen exercise protocols were effective in eliciting targeting heart rates as well as achieving a glycemic response from participants. The Freestyle Libre Pro flash glucose sensors and readers eliminated the need for sensor calibration, ultimately lowering participant burden and user-error. The sensor also allowed for free-living conditions and blinded participants to their glucose values, including no user alerts for values > 7.8 mmol/L or < 3.3 mmol/L. Objective physical activity and continuous caloric intake monitoring is also an asset as they provide a better understanding of day to day variations. Our findings also demonstrate high external validity as 50% of participants were able to participate from their homes thus demonstrating how aerobic HIIT can be implemented in a number of different settings. The present study also has increased generalizability to overweight and obese populations as our recruitment included 9 females (37.5%) with a pre-pregnancy BMI ≥ 25. It is also important to acknowledge that despite 3 - 20% of pregnant women developing GDM in Canada [54], no participants in our study reported it as a complication. Thus our sample did not have any metabolic complications that may have influenced the glucose values.

A limitation of our study was that it refrained from testing females before 20th week of gestation therefore the results are limited in their ability to address maternal response to HIIT throughout the entirety of pregnancy. In addition, a single bout of HIIT is unable to predict the cumulative effect of multiple sessions on maternal well-being. Our sample of pregnant individuals may also be subject to selection-bias given the high percentage of participants achieving physical activity guidelines and prior experience with HIIT. Due to the COVID-19 pandemic, mixed recruitment (i.e. in-person and online enrollment) and testing environments allowed for greater inconsistencies (e.g., type/model of bike, unregulated environmental temperatures, participant distractions). The flash glucose monitors utilized in the present study have demonstrated low accuracy of reporting glucose values when < 3.3 mmol/L, therefore our hypoglycemic values should be interpreted with caution [177]. Device malfunction and user-error (i.e., forgetting to apply accelerometer or battery failure, glucose sensor falling off) also contributed to limitations of the data, thus a mix-effect analysis was necessary. Although considered the 'gold-standard' for assessing physical activity, accelerometers are unable to differentiate between sitting and standing, with minutes of sedentary behaviour reported to be overestimates by 22.5% [214]. Self-reported data is also subjected to bias, as previously mentioned caloric intake journals are dependent on participant recall and have demonstrated inconsistencies compared to objective measures. Finally, the current study had limited diversity (i.e. mainly Caucasian, university educated, and without absolute contraindications to exercise) and therefore cannot be generalized to all pregnant individuals.

Future Directions

Our data presents the first empirical evidence of the 48-hour impact of aerobic HIIT on maternal glucose. However, there remains a number of important research gaps that need to be addressed. Based on the limited literature demonstrating altered maternal-fetal circulation with vigorous-intensity continuous exercise, future studies examining fetal response during acute bouts of aerobic HIIT are needed. Chronic interventions (e.g. performing HIIT three times per week for two to three weeks in accordance to previously published work; table 3) are also needed to determine the long-term effects of aerobic HIIT throughout pregnancy, including the long-term effect on maternal glycemic response and sleep duration. It is also worth investigating the rate in which nocturnal hypoglycemia may be occurring in non-diabetic normoglycemic pregnant individuals. Given our active and experienced sample of pregnant individuals, it is also important to explore the effects of HIIT in less active, novice populations. Previous meta-analyzed data, suggests that individuals with GDM would expect to see greater reductions in blood glucose after acute and chronic participation in exercise compared to pregnant females without metabolic disorders [15]. It is important to determine the effects of aerobic HIIT in pregnant populations diagnosed with GDM, as glycemic response is anticipated to be different. Furthermore, future research should also acknowledge different exercising modalities (e.g., treadmills), intensities and durations that could impact maternal response.

Chapter 7: Conclusion

To our knowledge, this is the first study to investigate the effects of aerobic HIIT on maternal glycemic response using a flash glucose monitor. Our findings demonstrated that 30-minutes of MICT had greater reductions in maternal interstitial fluid glucose than 19-minutes of HIIT, exemplifying the complexity of the dose-response relationship between exercise duration/intensity and maternal glucose consumption. Reassuringly, there were no significant difference in maternal glycemic responses over a 48-hour period with the exception that fewer participants experienced asymptomatic post-exercise hypoglycemia following HIIT compared to MICT. Our findings also suggest that in our small sample of pregnant individuals, aerobic HIIT eliciting intensities $\geq$ 90% of maternal HR_{max} appears to be well-tolerated and highly enjoyed by participants in comparison to MICT. Future research is necessary to determine the long-term effects of aerobic HIIT on maternal glycemic response, as well as adherence rates associated with perceived enjoyment. Compensatory behaviours (i.e., such as increased sedentary time or caloric intake) were not observed in this study. However, HIIT may acutely effect sleep durations for individuals struggling to achieve the recommended seven to nine hours of sleep per night. Interestingly, our data also identified a portion of pregnant individuals that may be prone to experiencing asymptomatic nocturnal hypoglycemia. Further investigation is needed to determine the cause and possible implications of nocturnal hypoglycemia in pregnant populations. Finally, with the growing number of individuals participating in HIIT after conception, there is an urgent call for more research on the safety and effects of HIIT.

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Appendices

Appendix A: *Health History Questionnaire*

HEALTH HISTORY QUESTIONNAIRE
PARTICIPANT ID #:
RESEARCHER INITIALS: DATE:

Date of Birth: ____/_____/____ **Height:** _____________ **Weight:** ____________

Due/Delivery Date: __________________ **Marital Status:** ____________________

Section A – Background Information:

1) What is your ethnic background?

- Caucasian
- Hispanic
- Aboriginal (please circle: First Nations, Métis, Inuit)
- Asian
- African American
- Other, please specify _______________

2) What education level did you complete? Please check all that apply.

- Elementary school
- High school
- College
- University (please circle: certificate, bachelor, master, doctorate)
- Other, please specify_______________

3) Postal Code _______

Section B – Health History:

Personal history is related to your own health. Family history is related to your immediate "Maternal" family (including your Mother and Father, your siblings or your other children) as well as the father of your children and his immediate family.

4) Please check **any and all** that apply:

Personal History **Family History**

Appendix B: *Physical Activity and Pregnancy Questionnaire*

0354

Office Use Only - ID# [| | |]

UMASS

Pregnancy Physical Activity Questionnaire

Instructions:
Please use an ordinary No. 2 pencil. *Fill in the circles completely. The Question will be read by a machine so if you need to change your answer, erase the incorrect mark* ***completely.*** *If you have comments, please write them on the back of the questionnaire.*

Example: During this trimester, when you are NOT at work, how much time do you usually spend:

E1. Taking care of an older adult

If you take care of your mom for 2 hours each day, then your answer should look like this... →

- ○ None
- ○ Less than 1/2 hour per day
- ○ 1/2 to almost 1 hour per day
- ○ 1 to almost 2 hours per day
- ● 2 to almost 3 hours per day
- ○ 3 or more hours per day

It is very important you tell us about yourself honestly. There are no right or wrong answers. We just want to know about the things you are doing during this trimester.

1. Today's Date: [|] / [|] / [| | |] (Month / Day / Year)
2. What was the first day of your last period? [|] / [|] / [| | |] (Month / Day / Year) ○ I don't know
3. When is your baby due? [|] / [|] / [| | |] (Month / Day / Year) ○ I don't know

---

During this trimester, when you are NOT at work, how much time do you usually spend:

4. **Preparing meals (cook, set table, wash dishes)**
   - ○ None
   - ○ Less than 1/2 hour per day
   - ○ 1/2 to almost 1 hour per day
   - ○ 1 to almost 2 hours per day
   - ○ 2 to almost 3 hours per day
   - ○ 3 or more hours per day

5. **Dressing, bathing, feeding children while you are sitting**
   - ○ None
   - ○ Less than 1/2 hour per day
   - ○ 1/2 to almost 1 hour per day
   - ○ 1 to almost 2 hours per day
   - ○ 2 to almost 3 hours per day
   - ○ 3 or more hours per day

Appendix C: *Pittsburgh Sleep Quality Questionnaire*

Subject's Initials______________ID#________________Date_____________Time_____AM PM

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?

   BED TIME ___________

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

   NUMBER OF MINUTES ___________

3. During the past month, what time have you usually gotten up in the morning?

   GETTING UP TIME ___________

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

   HOURS OF SLEEP PER NIGHT ___________

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

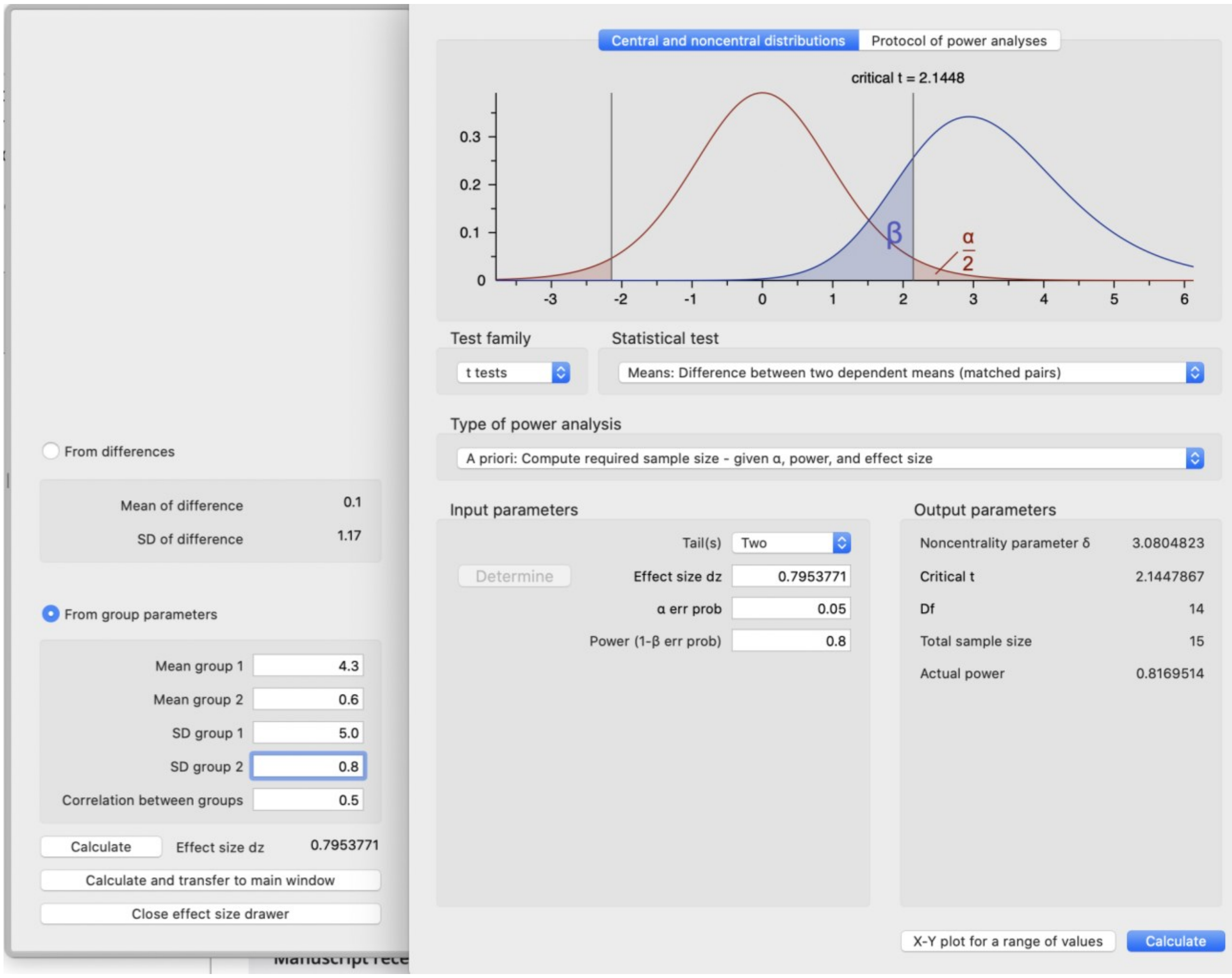
c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Appendix D: *Borg Rating of Perceived Exertion Scale*

Rating	Perceived Exertion
6	No exertion
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Appendix E: *G*Power Power Analysis*



Appendix F: *Rating of Perceived Enjoyment Scale*

<u>How do you presently feel about the physical activity you have just participated in? Please rank on the following scale:</u>

1. I hated it.
2.
3. I find it unpleasurable and/or boring
4.
5. Neutral.
6.
7. I find it pleasant and/or engaging
8.
9. I enjoyed it.
10.

Ranking for HIIT (high intensity interval training): __________

Ranking for MIC (moderate intensity continuous): __________