PHYSICAL ACTIVITY AND CARDIOMETABOLIC HEALTH IN EARLY PREGNANCY

ARE PHYSICAL ACTIVITY AND EXERCISE ASSOCIATED WITH CARDIOMETABOLIC HEALTH IN EARLY PREGNANCY?

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ABSTRACT

Background: Physical activity (PA) is an important component of a healthy pregnancy and has consistently been associated with improved weight management and a reduced risk of pregnancy complications. While the percentage of pregnant women meeting PA guidelines internationally is alarmingly low, no such data exists for the Canadian population. PA in pregnancy may also be a useful intervention for preventing and managing cardiometabolic dysfunction, but research in pregnancy is limited.

Objectives: 1) To describe the PA and exercise habits of women in early pregnancy and assess the percentage of women meeting SOGC/CSEP guidelines for exercise in pregnancy; 2) To determine the association of PA with maternal cardiometabolic health in early pregnancy.

Study Design: Maternal blood samples, and PA, dietary, and adiposity measures were collected from a subset of women in early pregnancy (12 – 17 wk gestation) upon enrollment in the Be Healthy in Pregnancy RCT. Fasted blood samples were analyzed for glucose, triglycerides, insulin, leptin, adiponectin and C-reactive protein (CRP). Self-reported and objectively measured PA were assessed using the PARmed-X for Pregnancy and an accelerometer. PA was quantified by three parameters: daily step count, energy expenditure (kcal/day) and meeting the SOGC/CSEP recommendations.

Results: For the 198 participants of age 31 ± 4 years; BMI 25.4 ± 4.7kg/m^2; at 13 ± 2 wk gestation (mean ± SD), 19.2% reported not exercising in early pregnancy. Approximately half of participants met the minimum SOGC/CSEP recommendation (15 min, 3x/wk), but only 14.2% met the preferred SOGC/CSEP recommendation (30 min, 4x/wk). Meeting

the preferred recommendation was associated with lower CRP. Daily step count and energy expenditure (kcal/day) were not significantly associated with glucose, triglycerides, insulin, leptin, adiponectin or CRP. Percent body fat and a higher diet quality were associated with some of the cardiometabolic biomarkers.

Conclusion: In a healthy pregnant cohort, while the majority had PA below recommendations, measured PA was not associated with most cardiometabolic biomarkers thus cardiometabolic risk in early pregnancy was low.

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"It's your place in the world; it's your life. Go on and do all you can with it, and make it the life you want to live." –Mae Jemison

TABLE OF CONTENTS

CHAPTER 5 – APPENDICES

FIGURES

TABLES

LIST OF ABBREVIATIONS

4-AAP – 4-aminoantipyrine

4-CP – 4-chlorophenol

3DDR – 3-day diet record

ACOG – American College of Obstetricians and Gynaecologists

ADP – adenosine diphosphate

ATP – adenosine triphosphate

BIA – bioelectrical impedance analysis

BMI – body mass index

BHIP – Be Healthy in Pregnancy

CRP – c-reactive protein

CSEP – Canadian Society for Exercise Physiology

CV – coefficient of variation

DAP - dihydroxyacetone phosphate

ELISA - enzyme-linked immunosorbent assay

EE – energy expenditure

G-3-P – glycerol-3-phosphate

G-6-P - glucose-6-phosphate

GDM – Gestational Diabetes Mellitus

GK – glycerol kinase

GPO – glycerol phosphate oxidase

GWG – gestational weight gain

H_2O_2 – hydrogen peroxide

HDL – high density lipoprotein

HCP – Health care provider

HRLMP – Hamilton Health Sciences Regional Laboratory Medicine Program

IOM – Institute of Medicine

FFQ – Food Frequency Questionnaire

HK – hexokinase

LED - light emitting diode

LDL – low-density lipoprotein

LGA – large-for-gestational age

LPL – lipoprotein lipase

MES – Maternity Experiences Survey

NAD – nicotinamide adenine dinucleotide

NADH – nicotinamide adenine dinucleotide reduced

NW – normal weight

OB – obese

OW - overweight

PA – physical activity

PARmed-X – Physical Activity Readiness Medical Examination

PHAC – Public Health Agency of Canada

Q1 – quartile 1

Q3 – quartile 3

RCT – randomized controlled trial

SD – standard deviation

SOGC – Society of Obstetricians and Gynecologists of Canada

TBW – total body water

TC – total cholesterol

TG – triglycerides

UW – underweight

CHAPTER 1

INTRODUCTION

CHAPTER 1 - INTRODUCTION

1.1 Rationale, objectives, and hypotheses

Pre-gravid obesity and excess gestational weight gain (GWG) remain major clinical challenges with greater than 50% of women entering pregnancy overweight and/or gaining excess weight during pregnancy.[1–5] Excess maternal weight is associated with marked increases in the risk of pregnancy complications such as hypertension, pre-eclampsia and gestational diabetes mellitus (GDM), as well as postpartum weight retention [2,3,5–7]; it is also the strongest predictor of offspring obesity.[5,8,9] Additional undesirable child health outcomes associated with excess maternal weight include macrosomia, hyperbilirubinemia, and hypoglycemia.[10] Unfortunately, many women do not receive proper counselling and fail to recognize the importance of weight gain regulation during pregnancy or are indifferent to such weight gain.[5,11]

Regular physical activity (PA) can help women manage their weight gain during pregnancy and it is recommended to all women without contraindications.[5,12] Internationally, the percentage of women that report being active during pregnancy is low, and the percentage that meet PA guidelines is even more concerning.[13] To our knowledge, there have not been any papers published on women's adherence to Canadian guidelines for PA in pregnancy. Such information is essential to determine the feasibility of implementing and promoting the current recommendations.

During pregnancy, there are normal adaptations in insulin sensitivity and secretion, glucose uptake, lipogenesis, and leptin and c-reactive protein (CRP) production to support the growth and development of the fetus.[14–18] Maternal obesity can lead to dysregulation

in these processes[19] and have adverse consequences for the mother and the fetus.[20] In a non-pregnant population, PA has been found to decrease the risk of insulin resistance and improve lipid profile, and has been associated with healthier circulating leptin and adiponectin.[21] In the pregnant population, a significant focus of this research has been on utilizing PA as a preventative and management tool for GDM, specifically assessing glucose tolerance and insulin sensitivity.[20–22] The effect of PA on other biomarkers of cardiometabolic health in pregnancy such as triglycerides, leptin, adiponectin, CRP, and body composition have received less attention and the findings have been inconsistent. There is a high degree of variability across study designs and there is currently no specific exercise prescription to improve cardiometabolic health in pregnancy.[20]

Given the identified gaps in knowledge, we aimed to determine the quantity and quality of the physical activity and exercise of women in early pregnancy and to perform an exploratory analysis to assess the association of physical activity with maternal cardiometabolic health.

Our first objective was to describe the physical activity and exercise habits of women in early pregnancy, and determine the percentage of women meeting the Society of Obstetricians and Gynecologists of Canada (SOGC)/Canadian Society for Exercise Physiology (CSEP) Clinical Practice Guidelines for Exercise in Pregnancy.

The second objective was to determine characteristics associated with higher odds of meeting the SOGC/CSEP recommendations.

The third objective was to assess differences in physical activity between pre-pregnancy BMI categories.

The fourth objective was to determine the association of step count with cardiometabolic biomarkers (glucose, insulin, triglycerides, leptin, adiponectin and CRP) in early pregnancy adjusting for important covariates.

The fifth objective was to perform sensitivity analyses for the association of energy expenditure (EE) and meeting SOGC/CSEP recommendations with cardiometabolic biomarkers (glucose, insulin, triglycerides, leptin, adiponectin and CRP).

Our hypotheses were that:

1. The majority of women will report being active during pregnancy, but a low percentage of participants will meet the SOGC/CSEP recommendations.
2. Multiparity and a higher pre-pregnancy BMI will be associated with lower odds of meeting the SOGC/CSEP recommendations.
3. Women in the overweight and obese category will have lower step counts and energy expenditure compared to women in the underweight and normal weight category.
4. Women that have a higher average daily step count will have a more favourable cardiometabolic profile, assessed by glucose, insulin, triglycerides, leptin, adiponectin and CRP.
5. Women that have a higher energy expenditure and meet the SOGC/CSEP recommendations will have a more favourable cardiometabolic profile, assessed by glucose, insulin, triglycerides, leptin, adiponectin and CRP.

1.2 Physical activity in pregnancy

1.2.1 Current recommendations and adherence

The guidelines for PA in pregnancy vary slightly across different international governing bodies (Table 1), but all emphasize the importance of remaining active while pregnant. Not being physically active during pregnancy puts women at risk of losing muscular and cardiovascular fitness, developing GDM, varicose veins and deep vein thrombosis, excess weight gain, poor psychological adjustments and a higher incidence of physical complaints.[12]

Table 1: Comparison of Canadian recommendations for physical activity during pregnancy

Agency	Type	Duration and Frequency	Intensity
Society of Obstetricians and Gynecologists of Canada/Canadian Society for Exercise Physiology (SOGC/CSEP)[12]	Aerobic and strength-conditioning exercises	Begin with 15 min. of continuous exercise 3x/week Increase to 30 min. sessions 4x/week	Maintain a conversation Target 12-14 on Borg's Scale
Public Health Agency of Canada (PHAC)[23]	Aerobic and strength-conditioning exercises Replace weight-bearing exercise with low-impact activities as pregnancy progresses	Build PA into your daily routine Gradually increase to 30-min. per session	Maintain a conversation

The Society of Obstetricians and Gynecologists of Canada (SOGC) and the Canadian Society for Exercise Physiology (CSEP) developed the Clinical Practice Guidelines for Exercise in Pregnancy (2003) to aid in the discussion of exercise between pregnant women and their health care providers (HCPs).[12] The SOGC/CSEP guidelines

recommend that women without contraindications continue to participate in aerobic and strength-conditioning exercises during their pregnancy with the goal to maintain a good fitness level, rather than reach peak fitness or train for an athletic competition (Table 1). The guidelines follow the FITT principle (frequency, intensity, type and time).[12,20] If women were previously sedentary, they should begin with 15 minutes of continuous exercise three times a week and gradually work up to 30-minute sessions four times per week. Modified target heart rate zones for aerobic exercise have been developed since there is a reduction in the maximal heart rate reserve for pregnant women.[12] The "talk test" and Borg's Rating of Perceived Exertion (Table 2) can also be used as measures of intensity. Women should exercise at an intensity that allows them to maintain a conversation and should reduce the intensity if this is not possible. A target of 12-14 on Borg's scale is suggested during pregnancy (Table 2).[24] Lastly, women should choose activities such as walking, stationary cycling, aquafit, or swimming which minimize the risk of loss of balance and fetal trauma. Women are recommended to avoid strength conditioning exercises that put them in the supine position after approximately 16 weeks' gestation.

Table 2: The SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy recommend using Borg's Rating of Perceived Exertion as a guideline for intensity of exercise during pregnancy

Borg's Rating of Perceived Exertion
6 7 very, very light 8 9 somewhat light 10 11 fairly light 12 13 somewhat hard 14 15 hard 16 17 very hard 18 19 very, very hard 20
Rating of 12-14 is appropriate for most pregnant women.

It is important that all women are medically screened before beginning or continuing an exercise program while pregnant.[20] The Physical Activity Readiness Medical Examination (PARmed-X) for Pregnancy (2015) was developed by CSEP to screen women interested in participating in PA during pregnancy and to facilitate awareness of the SOGC/CSEP guidelines. The 4-page document is completed by the patient and their HCP, and includes a pre-exercise health checklist, contraindications screening, and a health evaluation form for exercise clearance. The patient reports on their fitness/recreational activity habits during the past month using the FITT principle criteria, as well as their physical activity intentions while pregnant. The SOGC/CSEP Clinical Practice Guidelines are outlined in detail on the PARmed-X and both a

prescription for aerobic and muscular conditioning are included. The final page of the PARmed-X includes advice for active living during pregnancy and provides tips for staying active, eating healthy, and having a positive self and body image. Women with complicated pregnancies have been discouraged from participating in exercise activities for fear of impacting the underlying disorder or maternal and fetal outcomes.[12] Absolute contraindications that would preclude women from participating in exercise during pregnancy include: ruptured membranes, persistent 2nd or 3rd trimester bleeding, and high order multiple gestation (≥ triplets).[12] A list of relative contraindications has also been developed and includes conditions where the risks may exceed the benefits of regular physical activity, such as previous preterm birth or spontaneous abortion.[12]

The Public Health Agency of Canada (PHAC) has also released 'The Sensible Guide to a Healthy Pregnancy'[23] which encourages women to exercise during their pregnancy and recommends increasing active time to 30 minutes per session (Table 1). Fewer details are included outlining the frequency, intensity and type of activities compared to the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy.

Efforts should be made to harmonize the guidelines around the globe to avoid conflicting information. In the United States alone, the PA recommendations made by the American College of Obstetricians and Gynecologists (ACOG), Centers for Disease Control and Prevention (CDC), American College of Sports Medicine (ACSM), and United States Department of Health & Human Services (USDHHS) all differ slightly.[25] Despite slight variability among international guidelines, the consensus is that adherence rates are low.[21]

In an Irish population (n = 324), 22% of women in early pregnancy met the American College of Obstetricians and Gynecologists (ACOG) recommendation for Physical Activity and Exercise during Pregnancy (at least 150 minutes per week of moderate-intensity aerobic activity), and around 12% reported that they were not exercising.[26] Additionally, a study of 3482 women in Norway found that only 14.6% met the current guidelines for exercise in early pregnancy (20 min, 3x/wk).[27] Taken together, only a small percentage of women are meeting physical activity and exercise guidelines, and an alarming percentage of women report not exercising at all during their pregnancy. Low adherence to PA recommendations mainly stems from a lack of awareness of the guidelines, personal beliefs, and perceived barriers to exercise[25] (see details in Section 1.2.3). Studies generally show that there is greater adherence to PA during the first trimester and a tendency for PA levels to decrease during pregnancy.[25]

1.2.2 Benefits for mothers and their offspring

Being physically active during pregnancy impacts the health of the mother and should be encouraged by HCPs.[12] Exercising during pregnancy has been consistently associated with a reduced risk of preeclampsia, GDM, operative birth, and preterm birth, as well as a lower total weight gain and less fat mass gain.[13,28,29] Women that remain active during pregnancy also report improved pain tolerance, fewer depressive symptoms, and improved self-image.[13,27,30] Participating in regular aerobic exercise during pregnancy, such as a walking program, provides improvements in overall cardiovascular function, reduces resting blood pressure, and increases heart rate variability.[30,31]

Improved fetal health and a reduced risk of unfavourable health outcomes are also consistently associated with maternal exercise and physical activity during pregnancy.[32–35] In a systematic review of 28 randomized controlled trials (RCTs)[36], women that followed a structured exercise program during pregnancy had a 31% lower incidence of delivering a large-for-gestational age (LGA) or macrosomic baby. Reducing the number of LGA babies may lead to long-term improvements in offspring health, and a reduction in obesity risk and caesarean delivery rates.[20] Additional fetal adaptations that occur with maternal aerobic and strength training exercise include improved fetal heart rate adaptability, variability, and autonomic control.[20] A dose-response relationship between maternal exercise intensity and duration with fetal cardiovascular response has been suggested.[20]

1.2.3 Barriers for mothers

Women report several intrapersonal, interpersonal, and health barriers to remaining active during pregnancy.[25] Having a thorough understanding of these barriers and how they change throughout pregnancy is important for planning health promotion and preventative programs. Women commonly report a lack of time, energy, and motivation, child care difficulties, and lack of recreational facilities as barriers to staying active while pregnant.[25,27,28,37] Additionally, women report a lack of information from HCPs about appropriate exercise and a number of women have safety concerns about exercising during pregnancy. A residual dogma exists that exercise can lead to fetal hypoxia, fetal growth restriction resulting in low birthweight, hyperthermia and preterm delivery.[27,28] The SOGC and CSEP specifically state that participating in aerobic and strength training

exercise regimens during pregnancy does not increase the risk of adverse pregnancy or neonatal outcomes.[12] Participating in a structured exercise program has not been found to change the odds of delivering a small newborn or effect the gestational age at delivery, or lead to adverse outcomes.[28,36] The lack of information provided to women is a modifiable barrier that HCPs and public agencies can improve on. More research on what advice is provided to women by their HCPs and how women are utilizing this information is necessary.[38]

Physical limitations or restrictions are also frequently reported as barriers.[39] Some physiological barriers reported by women are: pregnancy symptoms (i.e. nausea), pain and discomfort (especially lower back and pelvis), change in the center of gravity, increased sense of breathlessness, and increased cardiorespiratory effort.[19,27,28,37,38,40]

1.3 Normal cardiometabolic adaptations in pregnancy

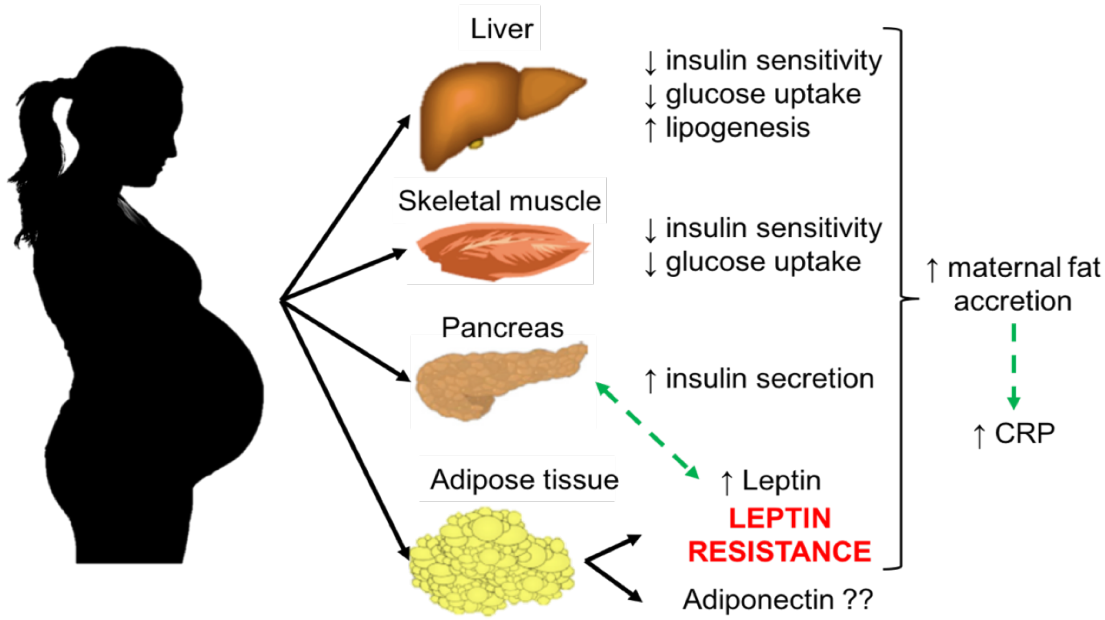
1.3.1 Glucose metabolism

Pregnancy is characterized as a diabetogenic state consisting of elevated serum insulin levels, slightly lower blood glucose levels, and peripheral insulin resistance.[20] Adaptations in glucose metabolism during pregnancy are necessary to supply the fetus with adequate glucose to promote its growth and development.[20,41]

During early pregnancy, basal glucose and insulin concentrations do not differ significantly from pre-gravid values[42] despite an increase in insulin secretion by the beta cells of the pancreas (Figure 1). The increase in insulin secretion[41] stimulates lipogenesis (fat formation) by the liver and reduces fatty acid oxidation.[20] This results in maternal fat accretion which is an important energy source later in pregnancy.[20]

Maternal insulin resistance at the skeletal muscle develops in the second trimester and peaks in the third trimester in response to placental hormones that decrease insulin sensitivity.[20,31,41,43] As a result, maternal uptake of glucose into the muscle cell decreases and results in an increase in maternal blood glucose concentration, which increases the glucose available for the fetus.[20,31,41] Insulin resistance leads to lipolysis (breakdown of lipids) which allows for the preferential use of fat by the mother to preserve available glucose and amino acids for the fetus.[41]

Figure 1: Maternal adaptations in metabolism and body composition in early pregnancy



*Adopted and modified from Park and Ahima. Metabolism. 2015;6(1):24-34.

1.3.2 Lipid metabolism

Changes in lipid metabolism during pregnancy promote maternal fat accretion in early and mid-pregnancy, and fat mobilization in late pregnancy.[42] Increased lipogenesis

and lipoprotein lipase (LPL) activity in early pregnancy[41,44] results in a steady increase in triglycerides.[41,42]

A decrease in LPL activity in the third trimester reduces fat uptake by adipose tissue and induces a state of maternal hyperlipidemia[44] with triglycerides rising to three times above non-pregnancy levels.[45] Enhanced lipolytic activity increases the availability of triglycerides to use as a maternal energy source.[44] The insulin-resistant condition and increase in estrogen are also associated with the development of hypertriglyceridemia.[45]

1.3.3 Adipokines – leptin and adiponectin

Adipose tissue is an endocrine and paracrine organ[41] that produces signaling molecules, including adipokines, that influence metabolic activity at other sites in the body including skeletal muscle, the liver and brain.[46] Adipokines (leptin, TNFα, IL-6, adiponectin) are important regulators of appetite, glucose homeostasis, and immune function.[43]

Leptin (the "satiety hormone")[43] is primarily secreted by adipocytes[46] and is important for the maintenance of whole body energy homeostasis.[15,43] In pregnancy, leptin is also produced by the placenta[21] and is critical for placental functioning and fetal development.[15,16] Hyperphagia, or excessive hunger, is commonly observed in pregnant women[44] and contradicts the satiating effects of leptin. This suggests that central leptin resistance may develop to increase energy stores for the fetus or compensate for insulin resistance in later gestation (Figure 1).[15,20,43]

Circulating leptin steadily increases during the first two trimesters and peaks in the late second or early third trimester (Figure 1).[15,16] Women with excess GWG have higher plasma leptin levels compared to women with low or adequate GWG.[47] Elevated plasma leptin levels, known as hyperleptinemia, is problematic and has been associated with an increased risk of developing GDM.[21]

Adiponectin is exclusively produced in adipose tissue and is an important mediator of insulin sensitivity and glucose homeostasis.[48] Unlike leptin, adiponectin plasma levels are inversely correlated with BMI and weight loss is associated with an increase in adiponectin in a non-pregnant population.[48,49] Because pregnancy is a state of insulin resistance, researchers are exploring adiponectin as a potential mediator of glucose metabolism through its insulin-sensitizing effects.[43,48] Aye, Powell and Jansson[50] proposed that increased levels of adiponectin in early pregnancy increases insulin sensitivity and enhances maternal fat (and nutrient) accretion, while declining adiponectin levels later in pregnancy decreases insulin sensitivity and promotes allocation of nutrients to the fetus via reduced glucose uptake in maternal peripheral tissues. Several studies have found lower adiponectin in women with GDM[48,51–54] which suggests hypoadiponectinemia in early pregnancy may predict the subsequent development of GDM. Contrary to the non-pregnant population, the association of maternal adiposity with adiponectin has been mixed, with some studies finding an association[55,56] and others not.[48,57–59]

1.3.4 Inflammatory profile - C-reactive protein

In addition to the metabolic adaptations discussed, pregnancy elicits a systemic inflammatory response, including an increase in circulating concentrations of CRP.[60,61] CRP is an acute phase reactant primarily produced by hepatocytes and activated by pro-inflammatory cytokines, such as IL-6 and TNF-α, in response to inflammatory stimuli.[61] CRP is also a marker of low-grade systemic inflammation, however the stimuli for production are not as well characterized.[61] Since adipocytes secrete IL-6[62], CRP is further elevated with maternal obesity[60,63] and excess inflammation is suggested to be involved in the pathogenesis of preeclampsia and GDM.[61] These inflammatory changes are believed to extend to the placenta and may predispose the fetus to a higher risk of metabolic disease in adulthood.[60,63]

1.4 Factors influencing cardiometabolic health in pregnancy

1.4.1 Adiposity

All metabolic and inflammatory markers previously discussed are negatively impacted by maternal obesity.[15,43,63] Not only does maternal obesity increase the risk of maternal metabolic complications, it also increases the risk of metabolic complications in the offspring later in life.[19,47,63] Higher levels of insulin, triglycerides, leptin, and CRP have been observed in overweight and obese pregnant women.[63,64] Additionally, excess GWG is a strong contributor to the risk of glucose intolerance and hyperleptinemia, regardless of pre-pregnancy BMI.[20,47]

1.4.2 Diet

Diet is a modifiable behavior that may significantly impact maternal cardiometabolic health.[65,66] Consumption of a high-quality diet rich in fruits, vegetables, whole grains and low fat dairy in pregnancy is associated with a more favourable cardiometabolic status, including lower levels of maternal glucose, insulin, and triglycerides.[66–68] Similarly, diets with a low-glycemic load[69] and reduced cholesterol[70] have reported smaller increases in triglycerides and decreased CRP when compared to control diets. These changes may benefit the mother by reducing immediate and long-term risk of cardiovascular disease[69] and provide a more favourable milieu for the developing fetus. Most often, dietary interventions are in tandem with an exercise intervention to assess the effect of an overall lifestyle modification.

1.4.3 Physical activity

Remaining physically active during pregnancy helps regulate metabolism, largely through enhanced weight control and reduced adipose tissue.[21] Maternal metabolic responses to physical activity vary across individuals and are influenced by dietary profile, the existing fitness level of the individual, and the intensity and duration of the activity.[20] Low compliance to interventions and variability in study methodology are significant challenges that exist in the field. More studies evaluating the type, timing, duration, and compliance of PA regimens are warranted to inform researchers of the relationship of PA in pregnancy on maternal cardiometabolic health.

1.4.3.1 Glucose and insulin

In response to muscle contraction during prolonged aerobic exercise, muscle glycogen is first used as an energy substrate.[20] As the length of exercise increases, liver glycogen stores are utilized to increase blood glucose to be used as an energy source.[20] Both insulin and exercise induce the translocation of the glucose transporter (GLUT4) from an intracellular location to the plasma membrane which increases the rate of glucose uptake by the skeletal muscle.[20,71] Since pregnancy is a state of insulin resistance, this exercise-induced glucose uptake may help women control their glucose levels and manage GDM.[20,72]

There is a large body of evidence on the improvements in glucose tolerance and insulin sensitivity with PA in pregnancy. A meta-analysis of 18 studies[22] reported that women classified as highly active before pregnancy or during pregnancy had significantly reduced odds of developing GDM. In a systematic review of eight PA interventions[31] three interventions improved glucose tolerance and insulin sensitivity.[73–75] Due to the low prevalence of GDM in the samples, these studies were not adequately powered to analyze the incidence of GDM by group. Adherence to the interventions were high (73-94%) which may explain the significant effect. Additional studies have reported improved insulin sensitivity and insulin response with PA in pregnancy.[76,77]

1.4.3.2 Triglycerides

A limited body of evidence supports the beneficial effect of PA on triglycerides in pregnancy. In an observational study (n = 925), mean plasma triglyceride concentrations were inversely related to habitual PA at 13 weeks gestation after adjusting for age, BMI,

and dietary variables.[45] Mean triglyceride concentration was lowest in the most active women compared to inactive women in early pregnancy.[45] The most active women were classified as: time performing PA (> 12.7hr/wk), energy expenditure (> 67.5 MET-hr/wk), or peak intensity (vigorous). Additional studies have reported similar associations of triglycerides with PA in pregnancy[21,77,78] while others have found a null effect.[21,79,80]

1.4.3.3 Leptin and adiponectin

There is evidence to support a decrease[81,82] and null change[79,83,84] in leptin concentrations with PA in pregnancy. An observational study (n = 879) in Washington, USA reported lower mean plasma leptin in women that reported participating in any recreational PA over a one week period in early pregnancy compared to women that were inactive.[81] In a small observational study[82] (n = 64), women that engaged in regular weight-bearing exercise (≥ 40 min., ≥ 4x/wk) throughout pregnancy had suppressed levels of leptin in each trimester compared to women that participated in non-weight bearing exercise. The studies finding a null effect reported low PA levels and low intervention adherence among participants which may have impacted their results.[79,83,84] Women in the control group in the BAMBINO trial[83] increased their PA throughout pregnancy compared to their initial assessment which reduced the power of the study to detect a difference. Collectively, these studies suggest that the inverse association between PA and leptin in pregnancy may only occur in women that are highly active.

To our knowledge, only one study has assessed the relationship of PA with adiponectin in healthy, pregnant women and the association was not significant.[79] Since both exercise and adiponectin have insulin-sensitizing effects, more research is warranted

to assess physical activity as a potential mediator of adiponectin levels in pregnancy and the possible benefit to maternal cardiometabolic health.

1.4.3.4 C-reactive protein

Few studies have been published on PA and CRP in pregnant women. Regular PA is suggested to reduce levels of pro-inflammatory cytokines (TNF-α and IL-6, increase levels of anti-inflammatory cytokines (IL-1 and IL-10), and reduce adipocyte-produced cytokines (IL-1 and TNF-α).[61,85] Together, these changes are proposed to diminish CRP production.[61] Data from observational studies suggests that active pregnant women have lower CRP levels compared to inactive women.[60,61,86] However, Wang et al.[61] found the association was no longer significant in an adjusted model (age, education level, weeks gestation, pre-pregnancy BMI, smoking and fruit consumption during pregnancy). Findings from an RCT (n=171)[87] showed a positive impact of a 12-week exercise intervention (following ACOG PA guidelines) beginning in early pregnancy on serum CRP concentrations, however it was not statistically significant. Differences in time points and methods used for PA assessment (i.e. self-reported vs. objectively measured) make it difficult to draw conclusions and more studies are needed.

1.5 Knowledge gaps

Studies evaluating PA in pregnancy commonly rely on subjective measures of PA such as physical activity recall questionnaires which are known to have bias, particularly with overreporting.[88] We will perform a comprehensive evaluation of PA and exercise in early pregnancy using both self-reported and objectively measured data. Additionally, to our knowledge, no other studies have assessed the percentage of pregnant women

meeting the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy using both subjective and objective measures of PA. This information is essential to determine the feasibility of implementing and promoting the current recommendations to pregnant women. Included in the PA assessment, we will determine characteristics associated with higher odds of meeting the SOGC/CSEP recommendations, and determine if there are differences in PA between BMI groups.

As presented, evidence on the association of PA during pregnancy with maternal cardiometabolic health is limited and inconsistent. There is an absolute lack of literature evaluating the association of PA recommendations with cardiometabolic health, and none to evaluate the SOGC/CSEP guidelines. We will address these gaps by assessing the association of three PA parameters (step count, EE, and meeting the SOGC/CSEP recommendations) with six cardiometabolic biomarkers (glucose, triglycerides, leptin, insulin, adiponectin and CRP). Additionally, we will control for adiposity and diet which are also known to influence cardiometabolic health.

CHAPTER 2

STUDY DESIGN AND METHODS

CHAPTER 2 – STUDY DESIGN AND METHODS

2.1. Study design and participants

Be Healthy in Pregnancy (BHIP) is a two-arm, three-site randomized controlled trial (NCT01689961) designed to assess the effect of a structured and monitored nutrition and exercise program (treatment) individualized to each woman for feasibility compared to standard prenatal care (control) on adherence to the IOM guidelines for GWG. Ethics approval was obtained from the Research Ethics Boards of Hamilton Health Sciences, Western University in London, and Joseph Brant Hospital in Burlington.

Healthy pregnant women were recruited from health care clinics by their health care providers in Hamilton, Burlington and London. Participants were informed about the BHIP study and consent to contact was obtained by completing a form containing participants' personal information, which was subsequently faxed to BHIP study staff. Recruitment poster advertisements were also placed in participating hospitals and at various locations in the community and included the BHIP email and phone number for women. A scripted screening phone call was used to determine if women were eligible according to inclusion/exclusion criteria (Table 3), to provide further information regarding the BHIP study and to schedule the first study visit between 12-17 weeks gestation (referred to as 'baseline'). Informed written consent was obtained from all participants at baseline and again once randomized. Participants were randomized via the 24-hr centralized online randomization service managed by the Biostatistics Unit at St. Joseph's Healthcare – Hamilton. Randomization was stratified by study site and pre-pregnancy BMI.

Recruitment for the BHIP study ended in March 2018 and a small number of participants are still in the intervention phase of the study. The data included in this thesis were collected at baseline prior to randomization and will not be analyzed by treatment group. Participants included in this analysis were a subset of the BHIP study sample with complete data sets available for all cardiometabolic biomarkers and physical activity parameters. Demographic information was collected at the first study visit via a questionnaire.

Table 3: Inclusion and exclusion criteria for the BHIP study

Inclusion Criteria	Exclusion Criteria
✓ Healthy pregnant females >18 years of age with singleton pregnancies (either nulliparous or multiparous) ✓ Less than 17 weeks gestation ✓ Pre-pregnancy BMI <40 kg/m^2 ✓ Plans to deliver at a Hamilton or London regional hospital or by home birth ✓ Able to tolerate dairy foods ✓ Approval of primary care provider (as indicated by PARmed-X) ✓ Able to provide signed informed consent	× Unable to understand some English × Type I or II diabetes × Known contraindications to exercise as recommended by Canadian clinical practice guidelines for pregnancy × Severe chronic gastrointestinal diseases or conditions × Refusal to consume dairy foods due to intolerance or dislike × Any significant heart, kidney, liver or pancreatic diseases × Currently smoking × A depression score above 12 on the validated Edinburgh depression questionnaire[89]

2.2. Assessment of physical activity in early pregnancy

2.2.1. PARmed-X for Pregnancy

The PARmed-X for Pregnancy (2003)[12] (see Appendix 1) was used as a screening tool for contraindication to exercise. Participation in the BHIP study was based on approval from the participant's health care provider upon study enrollment. It is also a

subjective, self-reported measure of women's activity in early pregnancy. In addition to reporting any contraindications, women were asked to report if they are currently exercising, along with the frequency, type, duration and intensity of the activities.

2.2.2 Accelerometer

Physical activity was also assessed at baseline using the SenseWear® armband tri-axis accelerometer (Model MF-SW; BodyMedia® Inc., Pittsburgh PA). Women were asked to wear the accelerometer for 72 consecutive hours (2 weekdays and 1 weekend day) on the back of the upper left arm (i.e. triceps), removing the device when showering, bathing, or swimming. The duration of any swimming was recorded on a separate questionnaire. Accelerometer data with a wear time > 10 hours per day was included in the analysis.[90–94]

The sensors in the device measure skin temperature, galvanic skin response, heat flux from the body, and movement. The physiological data are then processed using advanced algorithms to calculate energy expenditure, metabolic physical activity, and sleep duration (SenseWear® Professional 8.1 Software; BodyMedia® Inc., Pittsburgh PA) (see Appendix 2). Data on daily steps, energy expenditure, minutes of activity at specified MET intervals, and sleep duration were recorded (see Appendix 3). Upon comparing the distribution of the data points from each BodyMedia variable, average daily step count and average energy expenditure (kcal/day) resembled a normal distribution after a logarithmic transformation and were selected as PA parameters for the analysis. Previous literature has used these variables as measures of PA in pregnancy.[95–98]

2.2.3 Comparison to SOGC/CSEP Clinical Practice Guidelines

Data collected from the PARmed-X for Pregnancy and accelerometer were compared to the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy. The guidelines were divided into three categories: below recommendations (< 15min, 3x/week), minimum recommendation (≥ 15min, 3x/week - < 30min, 4x/week), and preferred recommendation (≥ 30min, 4x/week). The self-reported frequency, duration, and intensity of the activities on the PARmed-X were used to classify participants into one of the three categories. For the accelerometer, time spent at a moderate intensity [3 - <6 metabolic equivalents (METs)] per day was used to determine if participants met the minimum recommendation. The accelerometer data were not compared to the preferred recommendation which is expressed as 4 times per week, since only three days of data were collected.

2.3. Dietary assessment in early pregnancy

2.3.1. PrimeScreen Food Frequency Questionnaire

Participants completed the PrimeScreen Food Frequency Questionnaire (FFQ)[(99)] at baseline to assess diet quality. The PrimeScreen FFQ includes 25-questions to assess the intake of food, food groups, and beverages over the past month and was modified for BHIP to include additional questions on low-fat dairy intake. A dietary scoring protocol previously used by the Dana-Farber/Brigham & Women's Cancer Centre in a non-pregnant population was adapted for the BHIP PrimeScreen FFQ (see Appendix 4). Each subscale of answers was assigned a value, with the higher value representing the more healthful frequencies of intake based on current recommendations. An overall score

ranging from -34 (unhealthiest dietary pattern) to 69 (healthiest dietary pattern) was calculated for each participant. The score was included as a continuous variable in the analysis to control for variability in dietary quality.

2.3.2. 3-day diet record

Dietary intake was assessed at baseline using a standard three-day diet record (3DDR) that coincides with the same three days the accelerometer was worn. Participants were asked to record everything they consumed (food and beverages) for three consecutive days, including the amount, preparation method and brand (if applicable). Dietary analysis for macro- and micronutrient intake was conducted using the Nutritionist Pro™ Diet Analysis software, version 5.2.0 (Axxya Systems, Woodinville WA). Energy intake (kcal/kg/day) was included as a continuous variable in the analysis to control for diet quantity.

2.4. Anthropometry and body composition assessment

Height and weight were measured at baseline using a wall-mounted statiometer (Ellard Instrumentation, Monroe WA) and Tanita® BF-350 Body Composition Analyzer (Arlington Heights, IL) respectively. Pre-pregnancy BMI (kg/m^2) was calculated using current height and pre-pregnancy weight quantified as current weight subtracted from self-reported weight gain. Participants classified as underweight (UW) and obese (OB) were added to the normal weight (NW) and overweight (OW) categories, respectively.

Percent body fat (% BF) was measured by bioelectrical impedance analysis (BIA) using the Tanita® BF-350 Total Body Composition Analyzer. A single frequency electrical current is sent from four metal electrodes through the feet to the legs and

abdomen to determine the total conductor volume of the body.[100] Tissues with a higher water content (i.e. skeletal muscle) are more conductive than adipose tissue or bone, which the current meets with resistance (impedance). The impedance is measured and inputted into a Tanita® equation that has been validated in a non-pregnant population, which includes gender, age, height, and weight for improved accuracy. BIA has been shown to provide valid estimates of total body water (TBW) as compared to deuterium dilution in early pregnancy (14 weeks), but may not be as accurate in late pregnancy (32 weeks) due to increased hydration.[101] Percent body fat was included in the analysis as a continuous variable and pre-pregnancy BMI (UW/NW versus OW/OB) was included when the use of a categorical variable was more appropriate.

2.5. Laboratory procedures

Maternal fasted blood samples were collected at the baseline visit with a total volume of 19.5mL split into four vacutainers: serum (BD Vacutainer®) (10mL), SST™ serum separation tube (BD Vacutainer®) (5mL), sodium fluoride/ Na_2 ethylenediaminetetraacetic acid (EDTA) (BD Vacutainer®) (2mL) and PAXgene® Blood RNA Tube (PreAnalytix) (2.5mL). Samples were left to clot at room temperature (20-25° C) for 30 minutes; the PAXgene® tube was left at room temperature for a minimum of 2 hours (maximum of 72 hours). The serum tube, SST™ serum separation tube, and sodium fluoride/ Na_2 EDTA tube were centrifuged at 3000rpm for 10 minutes at 4°C; the SST™ Serum Separation tube was centrifuged for an additional 5 minutes. Samples were aliquoted and stored in polypropylene microcentrifuge tubes at -20°C for at least 24 hours before transfer to the - 80°C freezer.

2.5.1. Glucose and triglycerides

Glucose and lipid samples were prepared by BHIP study staff and analyzed by the Hamilton Regional Laboratory Medicine Program (HRLMP). Glucose analysis required plasma (500μL) collected from the sodium fluoride/ Na_2 EDTA vacutainer and lipid analysis required serum (500μL) from the SST™ serum separation tube. Normal and abnormal quality controls were run daily by HRLMP. Expected values of glucose and triglycerides are reported in Table 4.

Table 4: Reference ranges for cardiometabolic biomarkers of healthy pregnant women in early pregnancy

Analyte	**Reference Range**	**Citations**
Glucose[†]	4.1 – 5.6 mmol/L	Laboratory[(102)]
Triglyceride	0.5 – 1.8 mmol/L	Laboratory[(103)]
Leptin	11.3 – 63.7 μg/mL	From literature[(104)]
Insulin[†]	18.1 – 172.0 pmol/L	Laboratory[(105)]
Adiponectin	3.8 – 22.1 μg/mL	From literature[(106)]
CRP	< 8 mg/L	From literature[(107)]

[†]Reference range for non-pregnant women used as values in early pregnancy do not differ from pregravid.

Fasting plasma glucose was determined using a hexokinase photometric assay (Architect kit, Abbott, Abbott Park IL). The sample volume was 2μL and the assay coefficient of variation (CV) was ≤5%. The system was calibrated approximately every 30 days and the calibration curve ranged from 0.28 to 44.40 mmol/L. Samples were initially tested neat with a subsequent automatic dilution of 1:5 if values exceeded 44 mmol/L. Glucose was phosphorylated by hexokinase (HK) in the presence of adenosine

triphosphate (ATP) to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). G-6-P was then oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) to 6-phosphogluconate; nicotinamide adenine dinucleotide (NAD) was concurrently reduced to nicotinamide adenine dinucleotide reduced (NADH). For each micromole of glucose consumed, one micromole of NADH was produced. The quantity of NADH in the sample was detected via spectrometry as absorbed light at 340 nm (Abbott Architect *ci*4100, Abbott Park, IL).

Fasting serum triglycerides (TG) were analyzed using a glycerol phosphate oxidase photometric assay (Architect kit, Abbott, Abbott Park IL). The sample volume was 2.4μL and the assay CV was ≤5%. The system was calibrated approximately every 41 days and the calibration curve ranged from 0 to 16.05 mmol/L. Samples were initially tested with neat dilution factor and an automatic dilution of 1:4 was performed if values exceeded 16.05 mmol/L. TG were enzymatically hydrolyzed to free fatty acids and glycerol by lipase. Glycerol was then phosphorylated by ATP and glycerol kinase (GK) to produce glycerol-3-phosphate (G-3-P) and ADP. Next, G-3-P was oxidized by glycerol phosphate oxidase (GPO) to dihydroxyacetone phosphate (DAP) and hydrogen peroxide (H_2O_2) was produced. H_2O_2 reacted with 4-aminoantipyrine (4-AAP) and 4-chlorophenol (4-CP) to produce a red coloured dye whose absorbance (at 510nm) was proportional to the concentration of TG in the sample (Abbott Architect *ci*4100, Abbott Park IL).

2.5.2. Leptin, insulin, adiponectin and c-reactive protein

Fasting serum leptin and insulin were measured in duplicate by Luminex® human premixed multi-analyte enzyme-linked immunosorbent assay (ELISA; R&D Systems,

Minneapolis MN). Pooled plasma samples were run in triplicate on each plate as an internal quality control. A sample volume of 50μL was used and a 1:2 dilution factor was determined to be most appropriate. The Bio-Rad Bio-Plex® 200 system was calibrated prior to each use and validation was performed monthly. The intra- and interassay CVs were 5.7% and 15.6% for leptin, and 4.9% and 20.1% for insulin, respectively. Expected values of leptin and insulin of healthy pregnant women are outlined in Table 4.

Analyte-specific antibodies were pre-coated onto colour-coded magnetic microparticles and pipetted into wells along with standards and samples. The analytes of interest bound to the antibodies and unbound substances were washed away using a wash buffer (100μL) according to the protocol provided using a magnetic plate washer (Bio-Rad Bio-Plex Pro™ Wash Station). A human premixed biotin-antibody cocktail was added to each well and subsequently washed to remove unbound biotin. Streptavidin-phycoerythrin (Streptavidin-PE) was added to each well and bound to the biotinylated antibody and a final wash removed unbound Streptavidin-PE. The microparticles are resuspended in a buffer and read using the Bio-Rad Bio-Plex® 200. One light emitting diode (LED) classified the bead to determine the analyte of interest while a second LED determined the magnitude of PE-derived signal, which is in direct proportion to the amount of analyte bound.

Fasting serum adiponectin and CRP were measured by Luminex® premixed multi-analyte ELISA (R&D Systems) using the aforementioned ELISA protocol except a 1:500 dilution factor was used. The intra- and interassay CVs were 8.0% and 11.8% for

adiponectin, and 6.1% and 11.5% for CRP, respectively. Expected values of serum adiponectin and CRP in healthy pregnant women are detailed in Table 4.

2.6. Statistical analysis

Data analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM corp., Armonk, NY). Descriptive statistics were used to report characteristics of the study population and are presented as mean (SD), median (Q1, Q3), and count (%) as appropriate. Before any analyses were conducted, continuous variables were checked for normal distribution using the Shapiro-Wilk test and data was transformed accordingly (Table 5).

Table 5: List of variables included statistical analysis – variable type and data transformations described

Variable	**Type**	**Transformation**
Age	Continuous	None
Ethnicity	Categorical	None
Parity	Categorical	None
Percent body fat	Continuous	None
PrimeScreen diet score	Continuous	None
Total energy intake (kcal/kg/day)	Continuous	None
Average daily step count	Continuous	Logarithmic
Average energy expenditure (kcal/day)	Continuous	Logarithmic
Glucose	Continuous	None
Triglycerides	Continuous	Logarithmic
Leptin	Continuous	Logarithmic
Insulin	Continuous	Logarithmic
Adiponectin	Continuous	Logarithmic
CRP	Continuous	Logarithmic

Descriptive statistics were used to report the physical activity and exercise habits of participants and the percentage of participants meeting the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy (Table 6). Results are presented as median (Q1, Q3) and count (%) as appropriate.

Table 6: Criteria for the comparison of PARmed-X and accelerometer data to SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy to determine if participants are meeting the recommendations

Criteria category	Time spent at moderate intensity
Assessed by PARmed-X	
Below recommendation	< 15 minutes 3 times/week
Met minimum recommendation	≥ 15 minutes 3 times/week - < 30 minutes 4 times/week
Met preferred recommendation	≥ 30 minutes 4 times/week
Assessed by accelerometer[1]	
Below recommendation	< 15 minutes 3 times/week
Met minimum recommendation	≥ 15 minutes 3 times/week

[1]Accelerometer data were not compared to preferred recommendation since only three days of data were collected.

Univariable logistic regression was performed to determine factors associated with higher odds of meeting the preferred SOGC/CSEP recommendation (Table 6). The following variables were tested as possible factors: age (years), ethnicity (Caucasian versus other), parity (nulliparous versus parous), pre-pregnancy BMI (UW/NW versus OW/OB), and PrimeScreen diet score. The odds ratios (OR) are presented with 95%

confidence intervals (CI). Statistical significance was defined as a two-sided p-value of <0.05.

Daily step count, energy expenditure (kcal/day), and meeting the SOGC/CSEP recommendations were compared between pre-pregnancy BMI groups (UW/NW and OW/OB). The Mann-Whitney U test was performed for continuous variables with a non-normal distribution, and Pearson's chi-square test was performed for categorical variables. The Mann-Whitney U test was used to test for differences in average daily step count and energy expenditure (kcal/day) between UW/NW and OW/OB participants. The *U* statistic and p-value are presented along with the median (Q1, Q3). Pearson's chi-square tests were performed to compare the distribution of participants meeting the SOGC/CSEP recommendations (Table 6) between pre-pregnancy BMI groups (UW/NW and OW/OB). Separate chi-square tests were performed for data collected by PARmed-X and accelerometer. The chi-square (X^2) statistic and degrees of freedom (df) are presented along with count (%). Univariable logistic regression was performed to determine the magnitude and direction of significant associations. Statistical significance for the Mann-Whitney U test, Pearson's chi-square test, and univariable logistic regression was defined as a two-sided p-value of < 0.05.

The association between average daily step count and six cardiometabolic biomarkers (glucose, triglycerides, leptin, insulin, adiponectin and CRP) were explored by univariable regression. Additional univariable regressions were performed for the following variables with each cardiometabolic biomarker: age (years), ethnicity (Caucasian versus other), parity (nulliparous versus multiparous), % BF, PrimeScreen

diet score, and total energy intake (kcal/kg/day). Variables with $p < 0.05$ or deemed clinically significant were included in an adjusted model. Multivariable linear regression analysis was performed to explore the association between average daily step count and cardiometabolic biomarkers (glucose, triglycerides, leptin, insulin, adiponectin and CRP), adjusting for important covariates. The beta coefficient (β), 95% confidence interval (CI) and p-value for the unadjusted and adjusted models were calculated and statistical significance was defined as $p < 0.05$.

An additional multivariable linear regression was performed to assess the sensitivity of the association between average energy expenditure (kcal/day) and cardiometabolic biomarkers (glucose, triglycerides, leptin, insulin, adiponectin and CRP), adjusting for the same covariates previously deemed as significant. Multivariable linear regression was also performed to assess the sensitivity of the association between meeting the SOGC/CSEP recommendations (Table 6) and the aforementioned cardiometabolic biomarkers, adjusting for the same covariates previously deemed as significant. Separate models were used for SOGC/CSEP criteria assessed by PARmed-X and accelerometer.

CHAPTER 3

RESULTS

CHAPTER 3 – RESULTS

Section A: Assessment of physical activity in early pregnancy

A.3.1 Maternal characteristics

Of the 277 participants enrolled in the RCT, 198 with complete PARmed-X for Pregnancy and accelerometer data at baseline (study entry but prior to randomization) were included in the physical activity assessment (Table 7). The majority of participants were Caucasian, married, educated (completed post-secondary education), and had a total household income ≥ $75,000 (Table 7). Nearly half of participants were nulliparous and 45% were categorized as overweight and obese by pre-pregnancy BMI.

Table 7: Baseline demographic characteristics of study participants (n = 198) included in physical activity assessment

Characteristic	**Descriptive statistics**
Age (years) at enrollment*	31 (4)
Gestational age at enrollment (weeks)*	13 (2)
Pre-pregnancy BMI (kg/m^2)	
Underweight (< 18.5)	3 (1.5)
Normal weight (18.5 – 24.9)	106 (53.5)
Overweight (25.0 – 29.9)	54 (27.3)
Obese (≥30.0)	35 (17.7)
Education level	
College/trade school certificate or diploma	37 (18.7)
Bachelor's degree	63 (31.8)
Above Bachelor's degree	94 (47.5)
Other	4 (2.0)
Total annual household income	
<$30,000	7 (3.5)
≥$30,000 to <$75,000	42 (21.2)
≥$75,000	140 (70.7)
Prefer not to answer/don't know	9 (4.5)
Marital status	
Married	152 (76.8)
Common law/living with partner	37 (18.7)
Single	6 (3.0)
Not specified	3 (1.5)
Ethnicity	
Caucasian	184 (92.9)
Other	14 (7.1)
Parity	
Nulliparous (0 pregnancies)	95 (48.0)
Primiparous (1 pregnancy)	62 (31.3)
Multiparous (≥2 pregnancies)	40 (20.2)
Not specified	1 (0.5)

*Continuous variables with normal distribution presented as mean (SD).
Categorical variables presented as count (%).

A.3.2 Characterization of physical activity in early pregnancy

The self-reported exercise habits from the PARmed-X for Pregnancy questionnaire revealed that 80.8% of participants were currently exercising by participating in a variety of aerobic and strength training exercises (Table 8). Walking, resistance training, and yoga were most frequently reported. Most participants (52.8%) reported exercising 2-4 times per week, for 20-40 minutes per day (54.6%) and at a self-perceived medium intensity (67.5%). The accelerometer revealed considerable variability among participant's average daily step counts with steps ranging from 1903 to 17129 per day (Table 8). The energy expenditure measured by accelerometer ranged from 1384 to 3235 kcal/day (Table 8).

Table 8: Self-reported exercise on PARmed-X and objective assessment of physical activity by accelerometer at baseline (n = 198)

Physical activity	Descriptive statistics
PARmed-X	
Are you presently exercising?	
Yes	160 (80.8)
No	38 (19.2)
Frequency (times/week)	
1-2	44 (27.7)
2-4	84 (52.8)
4+	31 (19.5)
Time (minutes/day)	
< 20	11 (7.2)
20 - 40	83 (54.6)
40+	58 (38.2)
Intensity[1]	
Light	16 (10.0)
Medium	108 (67.5)
Heavy	90 (56.3)
Type of exercise[a]	
Walking	90 (58.4)
Resistance training	58 (37.7)
Yoga	40 (26.0)
Running	26 (16.9)
Biking	22 (14.3)
Swimming	13 (8.4)
Other[b]	55 (3.6)
Accelerometer	
Average daily step count*	6282 (5142, 8359)
Average energy expenditure (kcal/day)*	2028 (1866, 2292)

Categorical variables presented as count (%).
*Continuous variables with non-normal distribution presented as median (Q1, Q3).
[a]Categories are not mutually exclusive.
[b]Includes: unspecified cardio, hiking, organized team sports, rollerblading, fitness classes.

A.3.3 Comparison of self-reported and objective physical activity to SOGC/CSEP Clinical Practice Guidelines

Participants were removed from the analysis if missing data on frequency, duration, or intensity on the PARmed-X for Pregnancy (n =8) or time spent at moderate intensity from the accelerometer (n = 1). Based on self-reported exercise on the PARmed-X for Pregnancy, over half (56.8%) of participants reported exercising less than 15 minutes 3 times/week and therefore did not meet the recommendations outlined in the SOGC/CSEP guidelines (Table 9). The other 43.2% of participants reported exercise habits that met the minimum or preferred SOGC/CSEP recommendation. Of these women, only 14.2% met the preferred recommendation for exercise (Table 9). Based on the accelerometer data assessing time spent at a moderate intensity (3 - <6 METs), 56.9% of participants met the minimum recommendation as outlined by the SOGC/CSEP guidelines (Table 9). Including the time when the accelerometer was removed to swim (n = 14) did not modify the existing categories of these participants.

Table 9: Percentage of participants meeting recommendations outlined by the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy as assessed by the PARmed-X for Pregnancy (n = 190) and accelerometer (n = 197)

Criteria category	N (%)
Assessed by PARmed-X	
Below recommendation[a]	108 (56.8)
Met minimum recommendation[b]	55 (28.9)*
Met preferred recommendation[c]	27 (14.2)
Assessed by accelerometer	
Below recommendation[a]	85 (43.1)
Met minimum recommendation[d]	112 (56.9)

[a]Below recommendation = < 15 min 3 x/wk.
[b]Minimum recommendation = ≥ 15 min 3 x/wk - < 30 min 4 x/wk.
*Does not include participants that also met the preferred recommendation.
[c]Preferred recommendation = ≥ 30 min 4 x/wk.
[d]Minimum recommendation = ≥ 15 min 3 x/wk.

3.3.1 Characteristics associated with meeting the SOGC/CSEP recommendations

The results from the univariable logistic regression analyses are presented in Table 10. Age (years), ethnicity (Caucasian vs other), parity (nulliparous vs multiparous), and pre-pregnancy BMI (kg/m^2) were not significantly associated with higher odds of meeting the preferred recommendation (≥ 30 minutes 4 times/week) as outlined by the SOGC/CSEP guidelines. A higher PrimeScreen diet score (OR: 1.06; CI 1.00 - 1.12) was significantly associated with greater odds of meeting the preferred recommendation.

Table 10: Association of demographic and lifestyle characteristics with meeting the preferred SOGC/CSEP recommendation (≥ 30 minutes 4 times/week) assessed by PARmed-X for Pregnancy (n = 190)

Maternal characteristic	**OR**	**95% CI**	***p***
Age (years)	0.91	(0.18, 1.02)	0.100
Ethnicity (Caucasian) Reference level: Other	0.53	(0.07, 4.29)	0.553
Parity (multiparous) Reference level: nulliparous	0.85	(0.38, 1.93)	0.700
Pre-pregnancy BMI (kg/m^2)	0.92	(0.84, 1.02)	0.120
PrimeScreen diet score[a]	1.06	(1.00, 1.12)	**0.037**

Univariable logistic regression was performed using the following categories: below preferred recommendation (n = 163) vs met preferred recommendation (n = 27).
OR = odds ratio.
[a]Below recommendation (n = 128) versus preferred recommendation (n = 24).

A.3.4 Comparison of physical activity by pre-pregnancy BMI

Physical activity parameters were compared between women categorized by pre-pregnancy BMI as UW/NW and OW/OB (Table 11). Average daily step count did not significantly differ between UW/NW women (median = 6287) and OW/OB women (median = 6187) (Mann-Whitney U test, $U = 4785.5$, $p = 0.871$). Average energy expenditure (kcal/day) was significantly greater for OW/OB women (median = 2173) than UW/NW women (median = 1940) ($U = 2586.0$, $p < 0.001$). There was no difference between UW/NW and OW/OB groups in meeting the SOGC/CSEP minimum and preferred recommendations when assessed by PARmed-X (Pearson's chi-square test, $X^2(2) = 3.761$, $p = 0.152$) (Table 11). When assessed by accelerometer, there was a significant difference in the proportion of participants that met the minimum recommendation between pre-pregnancy BMI categories (Pearson's chi-square test, $X^2(2)$

= 7.698, $p = 0.006$) A univariable logistic regression was performed to determine the direction and magnitude of this association. Women classified as OW/OB had reduced odds of meeting the minimum recommendation assessed by accelerometer compared to UW/NW women (OR: 0.44; CI 0.25-0.79, p = 0.006).

Table 11: Comparison of physical activity parameters in underweight/normal weight and overweight/obese participants categorized by pre-pregnancy BMI

Physical activity parameter	**Underweight/Normal (n = 108)**	**Overweight/Obese (n = 89)**	***p***
Average daily step count*	6288 (5099, 8018)	6187 (5166, 8668)	0.871
Average energy expenditure (kcal/day)*	1940 (1761, 2132)	2176 (2009, 2483)	**<0.001**
Criteria category assessed by PARmed-X	**(n = 105)**	**(n = 85)**	0.152
Below recommendation[a]	62 (57.4)	46 (42.6)	
Met minimum recommendation[b]	25 (45.5)	30 (54.5)	
Met preferred recommendation[c]	18 (66.6)	9 (33.3)	
Criteria category assessed by accelerometer	-	-	**0.006**
Below recommendation[a]	37 (43.5)	48 (56.5)	
Met minimum recommendation[d]	71 (63.4)	41 (36.6)	

*Mann-Whitney U test performed for continuous variables with non-normal distribution ($p < 0.05$). Values reported as median (Q1, Q3).
Pearson's chi-square test performed for categorical variables ($p < 0.05$). Values reported as count (%).
[a]Below recommendation = < 15 min 3 x/wk.
[b]Minimum recommendation = ≥ 15 min 3 x/wk - < 30 min 4 x/wk.
[c]Preferred recommendation = ≥ 30 min 4 x/wk.
[d]Minimum recommendation = ≥ 15 min 3 x/wk.

Section B: Association of physical activity with cardiometabolic health

B.3.1 Maternal characteristics

A total of 162 participants with complete data sets for the PARmed-X for Pregnancy, accelerometer and cardiometabolic outcomes (glucose, triglycerides, leptin, insulin, adiponectin, and CRP) at baseline (study entry but prior to randomization) were included in the analysis. Demographic characteristics for this subset, including measures of adiposity and dietary parameters are presented in Appendix 5. Similar to the previous sample (n = 198), the majority of participants were Caucasian, married, educated (completed post-secondary education), and had a total household income ≥ $75,000 (see Appendix 5). Nearly half of participants were nulliparous and 44% were categorized as overweight and obese by pre-pregnancy BMI.

B.3.1.1 Physical activity parameters

Descriptive statistics for the physical activity parameters of participants included in the regression analyses (n = 162) are presented in Table 12. The variability in average daily step counts and energy expenditure was the same as previously mentioned with values ranging from 1903 to 17129 steps per day and 1384 to 3235 kcal/day (Table 12). Based on self-reported exercise on the PARmed-X for Pregnancy, over half (54.9%) of participants reported exercising less than 15 minutes 3 times/week and therefore did not meet the recommendations outlined in the SOGC/CSEP guidelines (Table 12). The remaining 45.1% of participants reported exercise habits that met the minimum or preferred SOGC/CSEP recommendation. Of these women, only 16.7% met the preferred recommendation (Table 12). Based on the accelerometer data assessing time spent at a

moderate intensity (3 - <6 METs), 57.4% of participants met the minimum recommendation as outlined by the SOGC/CSEP guidelines (Table 12).

Table 12: Physical activity parameters at baseline of participants (n = 162) included in the regression analysis

Physical activity parameter	**Descriptive statistics**
Average daily step count*	6254 (5199, 7972)
Average energy expenditure (kcal/day)*	2042 (1887, 2300)
Assessed by PARmed-X	
Below recommendation[a]	89 (54.9)
Met minimum recommendation[b]	46 (28.4)**
Met preferred recommendation[c]	27 (16.7)
Assessed by accelerometer	
Below recommendation[a]	69 (42.6)
Met minimum recommendation[d]	93 (57.4)

*Continuous variables with non-normal distribution presented as median (Q1, Q3). Categorical variables presented as count (%).
[a]Below recommendation = < 15 min 3 x/wk.
[b]Minimum recommendation = ≥ 15 min 3 x/wk - < 30 min 4 x/wk.
**Percent does not include participants that also met the preferred recommendation.
[c]Preferred recommendation = ≥ 30 min 4 x/wk.
[d]Minimum recommendation = ≥ 15 min 3 x/wk.

B.3.2 Cardiometabolic profiles

Cardiometabolic biomarker profiles of participants at baseline are presented in Table 13. Fasting values for plasma glucose, triglycerides and serum leptin were above the reference range for a small percentage (<10%) of participants. The majority of participants had serum CRP values below the reference range, and no participants had serum insulin or adiponectin values that exceeded the reference range.

Table 13: Cardiometabolic biomarker profiles of participants (n = 162) at baseline with cut-off values noted that were used to define outside the expected range for healthy women in early pregnancy

Cardiometabolic biomarkers	**Median (Q1, Q3)[1]**	**Reference range**	**Outside reference range N (%)**
Glucose† (mmol/L)	4.8 (4.5, 5.1)	4.1 – 5.6[(102)]	Above: 6 (3.7) Below: 5 (3.1)
Triglycerides (mmol/L)	1.2 (0.9, 1.5)	0.5 – 1.8[(103)]	Above: 15 (9.3) Below: 1 (0.6)
Leptin (μg/mL)	30.8 (12.9, 40.6)	11.3 – 63.7[(104)]	Above: 14 (8.6) Below: 35 (21.6)
Insulin† (pmol/L)	31.8 (21.3, 49.9)	18.1 – 172.0[(105)]	Above: 0 (0) Below: 26 (16.0)
Adiponectin (μg/mL)	8.7 (5.8, 10.9)	3.8 – 22.1[(106)]	Above: 0 (0) Below: 7 (4.3)
CRP (mg/L)	6.2 (2.5, 8.4)	< 8[(107)]	Above: 48 (29.6) Below: 0 (0)

†Reference range for non-pregnant women used as values in early pregnancy do not differ from pregravid.
[1]All values computed using untransformed data.

B.3.3 Association between physical activity and cardiometabolic markers

B.3.3.1 Physical activity assessed by average daily step count

The association between average daily step count and six cardiometabolic biomarkers were explored by univariable regressions (n = 162). In early pregnancy, average daily step count was not significantly associated with glucose, triglycerides, insulin, leptin, adiponectin or CRP (Tables 14-19). Additional univariable regressions were performed for the following variables with each cardiometabolic biomarker: age (years), ethnicity (Caucasian vs other), parity (nulliparous vs multiparous), % BF,

PrimeScreen diet score, and total energy intake (kcal/kg/day). Variables with $p < 0.05$ were included in the adjusted models. Age was deemed clinically important for cardiometabolic health[108] and was also included in the adjusted models.

Multivariable regression models were used to assess the association of average daily step count with the aforementioned cardiometabolic biomarkers, controlling for important covariates. The association of average daily step count with each cardiometabolic biomarker (glucose, triglycerides, insulin, leptin, adiponectin and CRP) remained non-significant in the adjusted models (Table 14-19). There were a few associations between covariates and cardiometabolic biomarkers that remained significant in the adjusted models. Percent body fat measured by BIA was positively associated with glucose ($\beta= 0.03$, $p<0.001$), triglycerides ($\beta= 0.01$, $p<0.001$), insulin ($\beta= 0.02$, $p<0.001$), leptin ($\beta= 0.04$, $p<0.001$), and CRP ($\beta= 0.02$, $p = 0.002$), and negatively associated with adiponectin ($\beta= -0.01$, $p<0.001$). Triglycerides were lower in Caucasian women compared to non-Caucasian women ($\beta= -0.11$, $p = 0.009$) and adiponectin was higher in Caucasian women compared to non-Caucasian women ($\beta= 0.12$, $p = 0.032$). Lastly, leptin was negatively associated with PrimeScreen diet score ($\beta= -0.01$, $p = 0.001$) in women with the same average daily step count.

Table 14: Linear regression analyses for the association of average daily step count and covariates with glucose (n = 162)

	Cardiometabolic biomarker			
	Glucose (mmol/L)			
	Unadjusted		Adjusted	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count[†]	0.05 (-0.36, 0.45)	0.825	0.08 (-0.30, 0.45)	0.686
Age (years)	0.01 (-0.10, 0.02)	0.425	-0.00 (-0.02, 0.02)	0.908
Ethnicity (Caucasian) Reference level: Other	0.01 (-0.25, 0.26)	0.940	-	-
Parity (multiparous) Reference level: nulliparous	0.06 (-0.07, 0.19)	0.364	-	-
Percent body fat[a]	0.03 (0.02, 0.04)	**<0.001**	0.03 (0.02, 0.04)	**<0.001**
PrimeScreen diet score[b]	-0.00 (-0.01, 0.01)	0.341	-	-
Energy intake (kcal/kg/day)[c]	-0.01 (-0.02, -0.01)	**<0.001**	-0.00 (-0.01, 0.01)	0.376

[†] Value log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), % BF, and energy intake (kcal/kg/day).

Table 15: Linear regression analyses for the association of average daily step count and covariates with triglycerides (n = 162)

	Cardiometabolic biomarker			
	Triglycerides† (mmol/L)			
	Unadjusted		Adjusted	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count†	-0.14 (-0.27, 0.00)	0.057	-0.11 (-0.24, 0.3)	0.121
Age (years)	0.00 (-0.01,0.01)	0.713	-0.00 (-0.01, 0.01)	0.744
Ethnicity (Caucasian) Reference level: Other	-0.12 (-0.21, -0.04)	**0.006**	-0.11 (-0.20, -0.03)	**0.009**
Parity (multiparous) Reference level: nulliparous	-0.02 (-0.06, 0.03)	0.519	-	-
Percent body fat[a]	0.01 (0.00, 0.01)	**<0.001**	0.01 (-0.20, -0.03)	**<0.001**
PrimeScreen diet score[b]	-0.00 (-0.01. 0.00)	0.077	-	-
Energy intake (kcal/kg/day)[c]	-0.00 (-0.00, 0.00)	0.345	-	-

† Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), ethnicity (Caucasian vs other), and % BF.

Table 16: Linear regression analyses for the association of average daily step count and covariates with insulin (n = 162)

	Cardiometabolic biomarker			
	Insulin[†] (pmol/L)			
	Unadjusted		**Adjusted**	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count[†]	-0.05 (-0.31, 0.20)	0.687	-0.03 (-0.26, 0.20)	0.804
Age (years)	-0.00 (-0.01, 0.01)	0.556	-0.01 (-0.02, 0.00)	0.089
Ethnicity (Caucasian) Reference level: Other	0.00 (-0.16, 0.16)	0.967	-	-
Parity (multiparous) Reference level: nulliparous	0.04 (-0.05, 0.12)	0.360	-	-
Percent body fat[a]	0.02 (0.01, 0.02)	**<0.001**	0.02 (0.01, 0.03)	**<0.001**
PrimeScreen diet score[b]	-0.01 (-0.01, 0.00)	0.119	-	-
Energy intake (kcal/kg/day)[c]	-0.01 (-0.01, -0.00)	**0.008**	0.00 (-0.01, 0.01)	0.967

[†] Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), %BF, and energy intake (kcal/kg/day).

Table 17: Linear regression analyses for the association of average daily step count and covariates with glucose (n = 162)

	Cardiometabolic biomarker			
	Leptin[†] (ng/mL)			
	Unadjusted		Adjusted	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count[†]	-0.13 (-0.48,0.21)	0.442	0.04 (-0.22, 0.30)	0.758
Age (years)	-0.00 (-0.02,0.01)	0.900	-0.01 (-0.02, 0.00)	0.221
Ethnicity (Caucasian) Reference level: Other	-0.44 (-0.26, 0.17)	0.684	-	-
Parity (multiparous) Reference level: nulliparous	0.10 (-0.01, 0.21,)	0.076	-	-
Percent body fat[a]	0.04 (0.03, 0.04)	**<0.001**	0.04 (0.03, 0.05)	**<0.001**
PrimeScreen diet score[b]	-0.01 (-0.02, -0.01)	**<0.001**	-0.01 (-0.02, -0.01)	**<0.001**
Energy intake (kcal/kg/day)[c]	-0.12 (-0.02, -0.01)	**0.001**	0.00 (-0.01, 0.00)	0.727

[†] Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), % BF, PrimeScreen diet score, and energy intake (kcal/kg/day).

Table 18: Linear regression analyses for the association of average daily step count and covariates with adiponectin (n = 162)

	Cardiometabolic biomarker			
	Adiponectin[†] (μg/mL)			
	Unadjusted		Adjusted	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count[‡]	0.13 (-0.05, 0.30)	0.165	0.09 (-0.08,0.26)	0.328
Age (years)	0.00 (-0.01, 0.01)	0.853	0.00 (-0.00, 0.01)	0.401
Ethnicity (Caucasian) Reference level: Other	0.12 (0.01, 0.23)	**0.036**	0.12 (0.01, 0.23)	**0.032**
Parity (multiparous) Reference level: nulliparous	-0.06 (-0.12, 0.00)	0.058	-	-
Percent body fat[a]	-0.01 (-0.01, -0.00)	**<0.001**	-0.01 (-0.01, -0.00)	**<0.001**
PrimeScreen diet score[b]	0.003 (-0.00, 0.01)	0.215	-	-
Energy intake (kcal/kg/day)[c]	0.00 (0.00, 0.01)	0.072	-	-

[†] Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), ethnicity (Caucasian vs other), and % BF.

Table 19: Linear regression analyses for the association of average daily step count and covariates with CRP (n = 162)

	Cardiometabolic biomarker			
	CRP[†] (mg/L)			
	Unadjusted		Adjusted	
Variables	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Average daily step count[‡]	-0.32 (-0.71,0.06)	0.096	-0.25 (-0.67, 0.17)	0.236
Age (years)	-0.01 (-0.025, 0.01)	0.257	-0.02 (-0.03, 0.00)	0.075
Ethnicity (Caucasian) Reference level: Other	-0.09 (-0.33, 0.15)	0.464	-	-
Parity (multiparous) Reference level: nulliparous	0.09 (-0.04, 0.22)	0.159	-	-
Percent body fat[a]	0.017 (0.01, 0.03)	**0.001**	0.02 (0.01. 0.03)	**0.002**
PrimeScreen diet score[b]	-0.01 (-0.02, -0.00)	**0.016**	-0.01 (-0.02, 0.00)	0.153
Energy intake (kcal/kg/day)[c]	-0.01 (-0.01, 0.00)	0.258	-	-

[†] Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]n = 160.
[b]n = 125.
[c]n = 161.
Adjusted for: age (years), % BF, and PrimeScreen diet score.

B.3.3.2 Physical activity assessed by average energy expenditure and meeting the SOGC/CSEP recommendations

A sensitivity analysis was performed to assess the association of energy expenditure with the six cardiometabolic biomarkers (glucose, triglycerides, insulin, leptin, adiponectin and CRP) (n = 162). Multiple linear regressions were performed and included

the covariates deemed significant or clinically important in Section 3.3.1. Average energy expenditure (kcal/day) was not significantly associated with glucose, triglycerides, insulin, leptin, adiponectin or CRP in the adjusted models (Table 20).

Table 20: Multivariable regression for the association of average daily step count energy expenditure with cardiometabolic biomarkers (n = 162)

	Physical activity parameters			
	Average daily step count[†]		**Average energy expenditure**[†] **(kcal/day)**	
Outcomes	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Glucose[a]	0.08 (-0.30, 0.45)	0.686	0.16 (-0.89, 1.22)	0.766
Triglycerides[†b]	-0.11 (-0.24, 0.3)	0.121	-0.19 (-0.58, 0.20)	0.333
Insulin[†a]	-0.03 (-0.26, 0.20)	0.804	-0.13 (-0.79, 0.53)	0.701
Leptin[†c]	0.04 (-0.22, 0.30)	0.758	-0.48 (-1.21, 0.26)	0.200
Adiponectin[†b]	0.09 (-0.08,0.26)	0.328	0.19 (-0.32, 0.69)	0.459
CRP[†d]	-0.25 (-0.67, 0.17)	0.236	-0.48 (-1.70, 0.74)	0.440

[†] Values log transformed prior to regression analysis.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]Adjusted for: age (years), % BF, and energy intake (kcal/kg/day).
[b]Adjusted for: age (years), ethnicity (Caucasian), and % BF.
[c]Adjusted for: age (years), % BF, PrimeScreen diet score, and energy intake (kcal/kg/day).
[d]Adjusted for: age (years), % BF, and PrimeScreen diet score.

An additional sensitivity analysis was performed to explore the association between meeting the SOGC/CSEP recommendations and the six cardiometabolic biomarkers (n = 162). The same covariates were included in the multiple linear regressions as those in

Section 3.3.1, and separate models were used for PA assessed by the PARmed-X and accelerometer. Glucose, triglycerides, insulin, leptin, and adiponectin were not significantly associated with meeting SOGC/CSEP recommendations when assessed by the PARmed-X for Pregnancy (Table 21). CRP was negatively associated with meeting the preferred SOGC/CSEP recommendation when PA was assessed by PARmed-X ($\beta = -0.23$, $p = 0.019$). When assessed by accelerometer, meeting the minimum SOGC/CSEP recommendation was not significantly associated with glucose, triglycerides, insulin, leptin, adiponectin or CRP.

Table 21: Sensitivity analysis by multivariable regression for the association of meeting SOGC/CSEP recommendations by PARmed-X and accelerometer with cardiometabolic biomarkers (n = 162)

	Physical activity parameters					
	PARmed-X for Pregnancy				**Accelerometer**	
	Met minimum recommendation* (n = 46)		**Met preferred recommendation* (n = 27)**		**Met minimum recommendation* (n = 93)**	
Outcomes	**β (95% CI)**	***p***	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Glucose[a]	0.04 (-0.10, 0.12)	0.572	0.02 (-0.16, 0.19)	0.840	0.05 (-0.07, 0.18)	0.407
Triglycerides[†b]	-0.04 (-0.09, 0.01)	0.131	-0.06 (-0.12, 0.00)	0.060	0.01 (-0.04, 0.05)	0.799
Insulin[†a]	-0.08 (-0.17, 0.01)	0.084	-0.05 (-0.16, 0.06)	0.340	-0.06 (-0.14, 0.02)	0.161
Leptin[†c]	-0.06 (-0.16, 0.04)	0.252	-0.08 (-0.20, 0.05)	0.215	-0.02 (-0.11, 0.07)	0.710
Adiponectin[†b]	0.03 (-0.03, 0.10)	0.348	0.05 (-0.03, 0.13)	0.204	-0.03 (-0.09, 0.03)	0.368
CRP[†d]	0.02 (-0.14, 0.19)	0.798	-0.23 (-0.43, -0.04)	**0.019**	-0.05 (-0.19, 0.10)	0.101

[†] Values log transformed prior to regression analysis.
*Reference level = below recommendation.
β = beta coefficient, CI = confidence interval, $p < 0.05$.
[a]Adjusted for: age (years), % BF, and energy intake (kcal/kg/day).
[b]Adjusted for: age (years), ethnicity (Caucasian), and % BF.
[c]Adjusted for: age (years), % BF, PrimeScreen diet score, and energy intake (kcal/kg/day).
[d]Adjusted for: age (years), % BF, and PrimeScreen diet score.

CHAPTER 4

DISCUSSION AND CONCLUSION

CHAPTER 4 – DISCUSSION AND CONCLUSION

4.1 Physical activity and exercise as a modifier of cardiometabolic health in early pregnancy

In this cohort of relatively healthy women, the amount of PA and exercise performed in early pregnancy was not significantly associated with cardiometabolic health as measured by blood glucose, triglycerides, leptin, insulin, and adiponectin. However, high physical activity indicated by those who met the preferred SOGC/CSEP recommendation (30 min, 4x/wk) was significantly associated with lower serum CRP, a marker of inflammation. Since only a small proportion of this cohort of pregnant women met the SOGC/CSEP guidelines, it is not surprising that the overall low levels of PA did not modify cardiometabolic health in early pregnancy.

Studies reporting a significant association of PA on cardiometabolic health are often those in which participants have reported high levels of or have been prescribed to a high-intensity exercise plan.[22,45,82,109] For example, an observational study of women in early pregnancy (n = 925) observed the lowest plasma triglyceride in the most active women compared to inactive women.[45] The most active women were classified as: time performing PA (> 12.7hr/wk), energy expenditure (> 67.5 MET-hr/wk), or peak intensity (vigorous). The study also reported a significant trend of decreasing plasma triglyceride with increasing PA (duration, energy expenditure, intensity), which was not observed in our study. In comparison to previous studies, the habitual PA performed by our participants was of a shorter duration and lower intensity, thus our findings suggest that a higher level of PA is needed to influence cardiometabolic health.

Unlike published studies to date, we assessed PA by three different methods: average daily step count, energy expenditure (kcal/day), and meeting the SOGC/CSEP recommendations (time spent at a moderate intensity). Neither of the two direct measures were associated with the six cardiometabolic biomarkers studied (glucose, triglycerides, insulin, leptin, adiponectin or CRP). The PA of women in our cohort was considered low when assessed by average daily step count.[110] Most participants (69.7%) were classified as sedentary (< 5000 steps/day) or low active (5000 – 7499 steps/day), and only a small percentage (12%) achieved 10,000 steps per day and were classified as active.[110,111] These step count indices were developed for healthy adults based on previous data that found an association between step counts and health conditions (i.e. adults with < 5000 steps/day were more likely to be classified as obese).[112] Our data supports the need for the BHIP exercise intervention, which encourages women to achieve 10,000 steps per day. The goal of 10,000 steps per day rose to popularity based on a 1965 Japanese pedometer that was called *manpo-kei*, which translates to 'ten thousand steps meter'.[112] Research studies have since emerged documenting the health benefits of attaining similar step counts and the goal of 10,000 steps/day has been incorporated into international PA guidelines.[110,112] In summary, the habitual step counts at baseline were low and were not significantly associated with improved cardiometabolic health.

With respect to average energy expenditure, the values observed in our cohort (2101 (SD = 326) kcal/day) were similar to those published in an observational study of pregnant women (2328 (SD = 894) kcal/day).[2] In the latter study[2], EE was calculated from participants' responses on the Pregnancy Physical Activity Questionnaire (PPAQ),

which may be biased to over-reporting and explain the higher mean and SD. While the EE of our cohort is comparable to the habitual PA performed by other Canadian women in early pregnancy[2], it is a level that does not appear to influence cardiometabolic health.

Using subjective and objective comparisons of meeting the minimum or preferred SOGC/CSEP Clinical Practice Guidelines also revealed that the level of PA performed was not significantly associated with glucose, triglycerides, insulin, leptin, or adiponectin. Only when women met the preferred SOCG/CSEP recommendation was lower serum CRP observed. This supports a study by Hawkins et al.[87] in which CRP in pregnant women was reduced after following a 12-week exercise intervention in which they were encouraged to follow the ACOG recommendations.

In summary, the observed PA in our cohort was not significantly associated with most cardiometabolic biomarkers in early pregnancy. The lack of achievement of the preferred recommendation in the majority of participants (83%) may be one explanation. Further, the majority of our sample presented with healthy lipid, glucose, insulin, and adiponectin profiles as few participants had values outside the normal range (Table 13). About 20% of participants had leptin values below the reference range, which is surprising given the known increase in circulating leptin during pregnancy.[15] The reference range for leptin was derived from the literature and a laboratory derived reference range should be developed. About one-third of participants presented with elevated CRP values (> 8 mg/L), which has previously been associated with adverse pregnancy outcomes.[107] The elevated CRP may be attributable to greater adiposity, as almost half of the participants in our sample were classified as overweight and obese. We

were not able to control for transient illnesses, such as a cold or flu, which would also increase serum CRP.[113] Overall, cardiometabolic health risk in our sample was low, and our findings suggest that PA may be more effective as an intervention when cardiometabolic dysfunction exists, as was seen with CRP.

4.2 Adiposity and diet quality influence cardiometabolic health in early pregnancy

Adiposity and diet quality both influenced some of the cardiometabolic markers. Percent body fat was positively associated with glucose, triglycerides, insulin, leptin, and CRP, and negatively associated with adiponectin. Elevated glucose, triglycerides, insulin, leptin and CRP have consistently been linked with maternal adiposity[20,47,60,63,64,114] and women with a higher %BF may be at risk of cardiometabolic dysfunction in pregnancy. Based on our findings, women with a higher %BF have lower serum adiponectin, and as a result may have reduced insulin sensitivity and be at risk of developing GDM. [55,56] As such, weight management is an important mediator of cardiometabolic dysfunction in pregnancy.[20,47,48,51–54,61]

A higher diet quality was weakly associated with lower serum leptin. A higher score on the PrimeScreen FFQ indicates that participants are consuming more fruits, vegetables, low-fat dairy, fish and lean meats, and less processed foods such as refined grains, sugar-sweetened beverages, and baked goods. Similar findings have been reported in the literature in a non-pregnant population. For example, in a study of 938 middle-aged healthy men and women, the highest compared to lowest quintile for whole-grain consumption was associated with 11% lower circulating leptin[115]; and in men and women from two tribes in Tanzania (n = 608), a diet high in fish was associated with

lower plasma leptin, independent of body fat and BMI.[116] It has been proposed that the relation between serum leptin and dietary patterns is confounded by energy intake and body weight; however, we found the association remained significant when adjusted for energy intake (kcal/day) and %BF.

Our findings contribute to the literature suggesting that an interplay of factors contributes to one's overall cardiometabolic health.[117] It is likely a combination of diet, exercise, and weight management that will have the largest impact on cardiometabolic health in pregnancy. Thus, we suggest that future research take a holistic approach rather than study variables in isolation.

4.3 Compliance with the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy

Low compliance (< 20% of subjects) with the SOGC/CSEP preferred recommendation aligns with previous studies that have compared PA in pregnancy to other international recommendations, although wide variation exists between different countries. Three studies compared PA measured either by questionnaires[118,119] or accelerometry[25] to the ACOG recommendations, which are slightly higher than the SOGC/CSEP preferred recommendations at ≥ 150 minutes per week of moderate-intensity aerobic activity. In a large Spanish study (n = 1,175) [118], 20% of women met the ACOG recommendation at 20 weeks' gestation, while in a smaller Spanish study (n = 133) [25], only 5% of women met the ACOG recommendation in both the first and second trimester. In a US study (n = 311)[119], 29% of women met the ACOG recommendation in their first trimester, which is nearly double what was reported in a previous US

population-based study.[120] The highest compliance reported was for a sample of Danish women (n = 7,915)[29] where 38% met the exercise recommendation in early pregnancy, as defined as ≥ 3.5 hours of exercise per week (Danish Health and Medicines Authority). It is commendable that over a third of women met the recommendation, which represents a much higher duration of PA than both the SOGC/CSEP and ACOG recommendations. In comparison to our cohort, notable lifestyle differences in the Danish women may explain the greater compliance with recommendations. For example, the average person in Copenhagen travels 2.4 km per day by bicycle[29] whereas Canadians are more reliant on motor vehicles. Thus, while our cohort was less active than the European studies, it was nearly identical in PA to the US population average.[120]

About half of participants met the minimum SOGC/CSEP recommendation (≥ 15 min, 3x/wk) indicating that this amount of activity is more feasible for most women than the higher preferred recommendation. It is not clear whether meeting the minimum recommendation is enough to confer health benefits for the mother and offspring. That being said, any time spent active is preferred over being sedentary.

We found that women with higher PrimeScreen diet scores were more likely to meet the preferred SOGC/CSEP recommendation. This suggests that women with healthier diets are also more conscious about remaining active during pregnancy. Previous studies have reported multiparity, a previous miscarriage, no engagement in PA before pregnancy, pre-pregnancy BMI, and a low education level to be associated with a lower probability of meeting exercise recommendations.[27,29] The limited diversity in demographics within our sample prevented us from assessing some of these

characteristics. We did not find age, ethnicity, parity or pre-pregnancy BMI were predictive of meeting the SOGC/CSEP preferred recommendation.

The impact of maternal adiposity status on achieving PA recommendations differed depending on the method of assessment. While the proportion of women meeting minimum or preferred recommendations was similar between pre-pregnancy BMI groups (UW/NW vs. OW/OB) when assessed by PARmed-X, assessment by accelerometer demonstrated that as pre-pregnancy BMI increased, the likelihood of meeting the minimum recommendation decreased. Such an inverse relationship was previously observed in a non-pregnant group of U.S. men and women (n = 3453), in which the percentage of participants achieving the US public health guidelines (≥ 30 min. of moderate intensity activity, ≥ 5x/wk) decreased across increasing BMI categories (NW, OW, and OB).[121] Overweight and obese individuals tend to over report PA on questionnaires[122], which may explain why the inverse association with BMI was only observed when PA was objectively measured.

4.3.1 *Comparison of PARmed-X for Pregnancy and accelerometer*

The objective (accelerometer) compared to the questionnaire assessment of PA resulted in a greater percentage of participants achieving the minimum recommendation. This difference may be attributed to the fact that the accelerometer measures physical activity which is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure"[123](p126), thus encompassing activity that occurs while at work, leisure (sports, household tasks, etc.), and sleeping. In contrast, the PARmed-X measures exercise, a sub-category of physical activity that is defined as "physical activity

that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective"[123](p128). The accelerometer captured activity beyond exercise including household tasks (i.e. cleaning, gardening), caregiving, and occupational activity. The PARmed-X asked about exercise and the frequency, duration, intensity, and type of activities. Because the accelerometer data is all encompassing, it is not surprising that a higher percentage of women achieved the SOGC/CSEP recommendations. It is also possible that women increased their activity level while wearing the accelerometer since they knew PA was being assessed.

An additional caveat in comparing the data is that the intensity reported on the PARmed-X for Pregnancy is subjective to the individual whereas moderate intensity on the accelerometer was objectively defined as 3 - <6 METs. There is the possibility that the self-perceived intensity of an activity may not coincide with the defined MET interval. Considering this, the data should not be interpreted as one method being superior to the other since they are measuring different constructs (physical activity vs. exercise).

4.4 Assessment of physical activity in early pregnancy

Most women in our cohort self-reported being active and participated in activities that are commonly reported by other pregnant women (i.e. bicycling, walking, running, strength training).[26,29,60] Such activities also aligned with those recommended in the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy. About 20% of our cohort reported not participating in any exercise in early pregnancy, which is very similar to what has previously been reported.[45,81,119] The percentage of women participating in

exercise may increase[27] once the nausea and fatigue associated with the first trimester subsides.[38]

4.4.1 Differences in step count and energy expenditure by pre-pregnancy BMI

Average daily step count of women in our study was similar between UW/NW and OW/OB participants, which is contrary to existing literature.[95] The step counts in our OW/OB group were higher than those reported in other literature, which may explain why we did not observe a difference by group. In a small UK study[124] (n = 58), OW and OB pregnant women had 500 fewer steps per day than that of our sample when measured by accelerometer. A larger discrepancy of over 1000 fewer steps in OW and OB women was observed in a study by Mottola et al.[125] (n = 65), which reported the mean daily step count from pedometers prior to beginning an exercise intervention in early pregnancy. A discrepancy in findings may be explained by differences in step counts measured by pedometers and accelerometers. In previous work, we found that pedometers gave a significantly higher reading than the accelerometer by about 1800-2000 steps in the 2nd and 3rd trimester (see Appendix 6). For the BHIP study, pedometers serve as a motivational tool for the intervention, and the accelerometer was used for a more accurate assessment of PA. Considering the differences in methodology, the true step counts in Mottola et al.[125] may have been even lower than the reported values. Thus, our cohort of OW/OB women are likely more physically active than the general pregnant population. Our findings lead us to hypothesize that compliance to the BHIP exercise intervention of 10,000 steps per day will be independent of pre-pregnancy BMI.

Daily energy expenditure (kcal/day) was higher in OW/OB women compared to UW/NW women, which is opposite to what was hypothesized. We predicted that UW/NW women would be more active, which would be reflected by a higher total daily energy expenditure.[126] However, due to a higher body mass and greater basal metabolic rate[127], total energy expenditure is higher in obese individuals.[2,121] Non-pregnant obese women expend an average of 28% more energy than normal weight women.[128] Future research should adjust for body composition when assessing total energy expenditure. Step count or time spent at a moderate intensity may be a better indicator of physical activity level if body composition data has not been collected.

4.5 Contributions to clinical practice

Our study is the first to assess compliance with the SOGC/CSEP guidelines using both subjective and objective PA assessment tools, and the findings are valuable for both HCPs and public health agencies. The majority of participants reported engaging in some form of exercise in early pregnancy, but there was a disconnect between this and meeting the SOGC/CSEP guidelines. Pregnancy is an opportune time for lifestyle modifications and our findings demonstrate there is room for improvement.[12,26] Health care providers should be encouraged to go through the PARmed-X for Pregnancy with their patients to facilitate awareness of the SOGC/CSEP guidelines and provide a platform to address women's questions or concerns. More guidance will eliminate a commonly reported barrier, which is a lack of education from HCPs about appropriate exercise.[38,40] In addition to clinical improvements, public health agencies should increase promotion of

the benefits of PA during pregnancy along with the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy.

4.6 Strengths and limitations

Our study has several strengths. The use of both subjective (PARmed-X for Pregnancy) and objective (accelerometer) measures of PA is unique and provided us with a thorough assessment of PA and exercise in early pregnancy. The accelerometer is considered the gold standard for PA assessment in a non-pregnant population and eliminates the bias associated with self-reported PA recall questionnaires.[88] Conducting a PA assessment in pregnancy using an objective measure is extremely valuable and our research provides new information on quantity of PA whereas previous studies were primarily based on self-reported data. Moreover, the accelerometer captures household and caregiving activities which are reported to contribute to 50-65% of total energy expenditure during pregnancy.[65] The accelerometer is also a feasible tool for pregnant women to use in a community-based research setting.[88]

The use of six different cardiometabolic biomarkers in the current study permitted a comprehensive approach to assess the association of PA with cardiometabolic health in early pregnancy and is unlike any published studies. Additionally, we controlled for multiple confounding variables, including the influence of both diet (quality and quantity) and adiposity on cardiometabolic health. Few PA studies in pregnancy collect data on diet and it is a strength that we were able to assess both diet quality (PrimeScreen diet score) and quantity (energy intake). We also controlled for maternal fat mass by measuring %BF via BIA, rather than only using a physical measure such as BMI.

Some limitations in the current study can be identified. Foremost, the analysis was observational and exploratory, and therefore causal relationships cannot be determined.

The demographics of our sample and recruitment location may limit the generalizability of our findings to the Canadian pregnant population. Most participants were Caucasian, well educated, and had a high household income (≥ $75,000). We are not certain that our findings would be replicated in a sample of non-Caucasian or low-income pregnant women. Previous reports have shown that low education, low income, and non-White race/ethnicity are related to reduced odds of participating in exercise or meeting recommendations for PA during pregnancy.[119] Participants were predominantly recruited to the BHIP study through midwifery clinics. Findings from the 2005/2006 Maternity Experiences Survey (MES) indicate that only 6.1% of women in Canada receive midwife-led prenatal care, and access varies by province.[129] In Ontario, 9.2% of women receive midwife-led prenatal care which is similar to that of British Columbia (9.8%) and Manitoba (9.4%).[129–131] In contrast, the total prevalence of midwife-led care across all Eastern provinces, Saskatchewan and the Yukon is only 0.3%. Further research is needed to determine factors associated with receiving midwife-led prenatal care in Canada. The current body of literature is limited to three studies in which the findings are inconsistent.[129–131]

The application of our measurement tools had some constraints. Unfortunately, the accelerometer was only worn for three days so we could not compare the accelerometer data to the preferred SOGC/CSEP recommendation over four days as we did with the PARmed-X for Pregnancy. Additionally, swimming is a preferred method of

exercise among pregnant women and would not be captured by the accelerometer since it cannot be worn in water. Water-based activities would not be reflected in the energy expenditure or time spent at a moderate intensity on the accelerometer but is reported on a separate questionnaire. Lastly, the version of the PrimeScreen FFQ that has been adapted for the BHIP study and the corresponding scoring protocol have not yet been validated in a pregnant population.

4.7 Future directions

The exploratory study sets the framework for the future analysis of the BHIP randomized trial. The longitudinal assessment of PA throughout pregnancy with and without the structured exercise intervention will determine if guidance can assist women to meet current PA recommendations. Previous studies have consistently shown that PA levels decline as pregnancy progresses[28,40,65,132], particularly among women who are overweight or obese.[65] In the BHIP sample, PA throughout pregnancy and into the post-partum period can be assessed using both subjective (exercise questionnaire) and objective (accelerometer and pedometer) measures. Additionally, it can be determined if the change in PA is consistent across different PA parameters (i.e. self-reported activity, step count, energy expenditure, meeting SOGC/CSEP recommendations). As discussed, there are several strengths associated with the accelerometer and it should be used as the primary PA assessment tool in the future analyses of BHIP.

A longitudinal assessment of cardiometabolic health during pregnancy and at six months post-partum will be performed in the BHIP sample. The changes across multiple cardiometabolic biomarkers can be studied and additional biomarkers, including total

cholesterol (TC), high-density lipoprotein (HDL) and low density lipoprotein (LDL), will be included in future analyses. We will further explore the association of PA assessed by multiple PA parameters with cardiometabolic health across pregnancy and into the post-partum period. Future analyses can also be conducted by group allocation to determine if there is a causal association between the exercise and diet intervention and cardiometabolic health.

Outside of the BHIP study, the goal of future research should be to increase habitual PA and exercise engagement in pregnant women. Foremost, researchers must evaluate the information and resources currently provided to pregnant women by their HCPs, and determine what is lacking from the patient's perspective. From here, it can be determined whether implementing a new approach increases awareness and compliance with the SOGC/CSEP Clinical Practice Guidelines for Exercise in Pregnancy. An additional question to be answered by future research is whether PA in pregnancy must be in bouts of exercise to confer health benefits, as recommended by the SOGC/CSEP, or whether overall activity level is as effective.

CHAPTER 5

APPENDICES

CHAPTER 5 - APPENDICES

5.1 Appendix 1 – PARmed-X for Pregnancy (2003) used in the BHIP study

PHYSICAL ACTIVITY READINESS EXAMINATION FORM (PARmed-X for pregnancy)
B-HIP RESEARCH STUDY

Department of Pediatrics, McMaster University
Phone 905-525-5146 ext. 22967
Fax 905-308-7584

Name: _____ **Physician/Midwife Name:**
_____
Address: _____ **Phone #:**
_____
Phone #: (W): _____
(H): _____ **Birth Date:** _____

Healthy women with uncomplicated pregnancies can participate in properly designed physical fitness programs without significant risk to themselves or their unborn child. Postulated benefits of such programs include improved aerobic and muscular fitness, promotion of appropriate weight gain, improved mood state and body image. Regular exercise may also help to prevent gestational glucose intolerance and pregnancy-induced hypertension. The safety of prenatal exercise programs depends on an adequate level of maternal-fetal physiological reserve. PARmed-X for Pregnancy is a convenient checklist for use by physicians and midwives to evaluate pregnant patients who want to enter a prenatal fitness program and for ongoing medical surveillance of exercising patients. **If the patient's health status changes as pregnancy progresses, the physician or midwife is encouraged (if appropriate) to withdraw clearance to exercise by calling the B-HIP Research Office at 905-521-2100 ext. 22967; FAX 905-308-7548.**

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PRE-EXERCISE HEALTH CHECKLIST
(TO BE COMPLETED BY PARTICIPANT)

PART A: GENERAL HEALTH
(past month)
In the past, have you experienced:
If **YES,**
(**Circle #**)
fitness/recreational activities:
1. Miscarriage in an earlier pregnancy?
_____
2. Other pregnancy complications?
3. Heart trouble?
4. Chest pain or palpitations?
workout-type:
5. Breathing problems? (e.g. Asthma, bronchitis)
4 4+
6. Dizziness/fainting?
20-40 +40
7. High blood pressure?
Heavy_____
8. Diabetes?
Medium_____
9. Arthritis or other problems with joints?
Light_____
10. Other health problems which might affect your ability to exercise?
involve:

PART B: CURRENT STATUS

Due Date: _____

Date of last menstrual period:

_____

During this pregnancy have you experienced: (**Circle #**)
1. Marked fatigue?
2. Bloody discharge from the vagina (e.g. spotting)?
3. Unexplained fainting or dizziness?
4. Unexplained abdominal pain?
5. Sudden swelling of ankles, hands or face?
6. Persistent headaches or problems

PART C: HEALTH HABITS

1. Are you presently exercising?

please list any

If **NO,** go to question #**3**.

2. Please check off your

Frequency (#/ week) **1-2 2-**
Time (min./day) **<20**
Intensity

3. Does your regular occupation

(PLEASE TURN OVER)

CONTRAINDICATIONS

(TO BE COMPLETED BY ATTENDING HEALTH CARE PROVIDER)

ABSOLUTE CONTRAINDICATIONS

Permanent of temporary restriction until condition is treated, stable and/or past acute phase. Please **circle** any that pertain to your patient:

1. Clinically significant valvular or ischemic heart disease?
2. Uncontrolled Type I diabetes mellitus, peripheral vascular disease, thyroid disease, hypertension, or other systemic disorders (hepatitis, mononucleosis, etc.).
3. An incompetent cervix (multigravida patients)?
4. A history of two or more spontaneous abortions?
5. Persistent 2nd and 3rd trimester bleeding/placenta previa?
6. Ruptured membranes or premature labour?
7. Toxemia or pre-eclampsia (current pregnancy)?
8. Evidence of fetal growth restriction (current pregnancy)?
9. A multiple pregnancy (eg. Triplets)?

RELATIVE CONTRAINDICATIONS

Risks may exceed benefits of fitness conditioning. Decision to exercise or not should be made with qualified medical advice. Please **circle** any that pertain to your patient:

1. History in previous pregnancies of premature labour and/or spontaneous abortion?
2. Anaemia or iron deficiency (Hb.<1.0 g/d)
3. Clinically significant pulmonary disease (e.g. COPD)?
4. Mild valvular or ischemic heart or respiratory disease, e.g. chronic hypertension, asthma.
5. Very low physical fitness prior to pregnancy?
6. A prescription of drugs which can alter cardiac output or blood flow distribution?
7. Obesity and/or 'Type II' diabetes prior to pregnancy?
8. Very low % of body fatness, eating disorders (i.e. anorexia or bulimia)?

(Taken from: Wolfe, L and Mottola, MF. 2002. PARmed-X for Pregnancy. Available from the Canadian Society of Exercise Physiology. www.csep.ca)

5.2 Appendix 2 – Downloading data from BodyMedia® SenseWear® armband data

The SenseWear® Professional 8.1 Software (BodyMedia® Inc., Pittsburgh PA) is used to extract and analyze data from the BodyMedia® SenseWear® armband. Height, weight, and birth date are entered for each participant, and a report is produced (see Appendix 4).

The algorithms used by the SenseWear® software were developed using a data driven machine learning approach. Detailed information on the process to develop the algorithms is outlined in Andre et al.[133] The algorithms in the software utilize the physiologic signals from the sensors on the device (tri-axial accelerometer, skin temperature, galvanic skin response, and heat flux) to detect the wearer's context for each minute of time. The device's ability to detect context is important to accurately predict measures such as step count and energy expenditure. BodyMedia's algorithms analyze activities by their fundamental components such as walking, running, resting, sleeping, resistance, and lower-leg motion. For each fundamental component, a different equation is used to predict energy expenditure. From this, physical activity duration and METs levels can be determined.

5.3 Appendix 3 – Accelerometer report generated by SenseWear® Software

A report is generated for each participant with multiple measures for each day the accelerometer was worn. Daily step count, total energy expenditure, and time spent at a moderate intensity were used in our analysis.

SenseWear Report Created Wed Sep 19, 2012 Page 1 of 1

enabled by BODYMEDIA

Clinician / Physician	Hospital / Organization	Practice / Department

Subject	Age	Gender	Weight	Height	Handed	Smoker	BMI
Ann	29	Female	134.0 lbs (60.8 kg)	5' 2" (157 cm)	Right	No	24.67

Start Time	End Time	Duration of View	Duration on-body
Wed Sep 12, 2012 08:56 AM	Sat Sep 15, 2012 08:04 AM	2 days 23 hrs 8 min	2 days 20 hrs 35 min (96.4%)

* Partial Day. Value is not representative of a 24-hour timeframe.

The information contained within this report is not to be used for diagnostic purposes.

5.4 Appendix 4 – Calculating PrimeScreen FFQ[99] diet score

Higher positive values indicate more healthful dietary behaviors. Negative values indicate less healthful dietary behaviors. Values were summed to generate the diet quality score.

The questions below are designed to help us understand your eating behaviors and food choices. There are no clear right or wrong answers. Please choose the answer that best describes your eating habits over the last month**.** How often do you eat …

1. Dark green leafy vegetables (spinach, romaine lettuce, mesclun mix, kale, turnip greens, bok choy, swiss chard):
   - Less than once per week …… 0
   - Once per week …….. 1
   - 2-4 times per week…… 2
   - Nearly daily or daily …… 3
   - Twice or more per day…… 4

2. Broccoli, broccoli rabe, cauliflower, cabbage, brussel sprouts:
   - Less than once per week…….. 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

3. Carrots:
   - Less than once per week…… 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

4. Other vegetables (e.g. peas, corn, green beans, tomatoes, squash):
   - Less than once per week…… 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

5. Citrus fruits (e.g. oranges, grapefruits):
   - Less than once per week…… 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

6. Other fruits (e.g. fresh apples or pears, bananas, berries, grapes, melons):
   - Less than once per week…… 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

7. Whole milk dairy foods (whole milk, hard cheese, butter, ice cream):

Less than once per week……	0
Once per week …….	-1
2-4 times per week ……	-2
Nearly daily or daily……	-3
2 – 3 times per day……	-4
4 - 6 times per day……	-5

8. Low-fat milk (e.g., skim, 1%, 2%):

Less than once per week……	0
Once per week …….	1
2-4 times per week ……	2
Nearly daily or daily……	3
2 – 3 times per day……	4
4 - 6 times per day……	5

9. Low-fat Greek yogurt (0%, 2%):

Less than once per week……	0
Once per week …….	1
2-4 times per week ……	2
Nearly daily or daily……	3
2 – 3 times per day……	4
4 - 6 times per day……	5

10. Low-fat regular yogurt:

Less than once per week……	0
Once per week …….	1
2-4 times per week ……	2
Nearly daily or daily……	3
2 – 3 times per day……	4
4 - 6 times per day……	5

11. Cottage cheese:

Less than once per week……	0
Once per week …….	1
2-4 times per week ……	2
Nearly daily or daily……	3
2 – 3 times per day……	4
4 - 6 times per day……	5

12. Fortified milk alternatives (e.g. soy, almond, rice milk):

Less than once per week……	0
Once per week …….	1
2-4 times per week ……	2
Nearly daily or daily……	3
2 – 3 times per day……	4
4 - 6 times per day……	5

13. Whole eggs:

Less than once per week……	0
Once per week ……..	1
2-4 times per week …….	2
Nearly daily or daily……	3
Twice or more per day……	-1

14. Dried beans, split peas or lentils:

Less than once per week……	0
Once per week ……..	1
2-4 times per week …….	2
Nearly daily or daily……	3
Twice or more per day……	4

15. Nuts and/or nut butter (e.g. peanut, almond, soy butters):

Less than once per week……	0
Once per week ……..	1
2-4 times per week …….	2
Nearly daily or daily……	3
Twice or more per day……	4

16. Beef, pork or lamb:

Less than once per week……	0
Once per week ……..	-1
2-4 times per week …….	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

17. Processed meats (sausages, salami, bologna, hot dogs, bacon):

Less than once per week……..	0
Once per week ……	-1
2-4 times per week …….	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

24. Deep fried foods:

Less than once per week……. 0
Once per week …… -1
2-4 times per week ……. -2
Nearly daily or daily…… -3
Twice or more per day…… -4

25. How often do you add salt to food at the table?

Less than once per week……. 0
Once per week …… -1
2-4 times per week ……. -2
Nearly daily or daily…… -3
Twice or more per day…… -4

Total: _____

RATING SCALE: Continuous variable – higher score = healthier diet

Adapted from the PrimeScreen Questionnaire, President and Fellows of Harvard College, Harvard School of Public Health,

Copyright 1999

Source: Rifas-Shiman, SL, Willett, WC et a.l PrimeScreen, a brief dietary screening tool reproducibility and comparability with both a longer food frequency questionnaire and biomarkers. *PubHealNut.*1999:4 (2), 249-254

5.5 Appendix 5 - Demographic characteristics of participants at baseline (n = 162) included in regression analysis

Characteristic	Descriptive statistics
Age (years) at enrollment*	31 (4)
Gestational stage at enrollment (weeks)*	13 (2)
Education level	
College/trade school certificate or diploma	32 (19.8)
Bachelor's degree	48 (29.6)
Above Bachelor's degree	81 (50.0)
Other	1 (0.6)
Total annual household income	
<$30,000	7 (4.3)
≥$30,000 to <$75,000	36 (22.2)
≥$75,000	112 (69.1)
Prefer not to answer/don't know	7 (4.3)
Marital status	
Married	121 (74.7)
Common law/living with partner	33 (20.4)
Single	6 (3.7)
Not specified	2 (1.2)
Ethnicity	
Caucasian	150 (92.6)
Other	12 (7.4)
Parity	
Nulliparous (0 pregnancies)	80 (49.4)
Primiparous (1 pregnancy)	48 (29.6)
Multiparous (≥2 pregnancies)	33 (20.4)
Not specified	1 (0.6)
Adiposity	
Pre-pregnancy BMI ($kg/m^{2)}$	
Underweight (< 18.5)	3(1.9)

Normal weight (18.5 – 24.9)	88 (54.3)
Overweight (25.0 – 29.9)	44 (27.2)
Obese (≥30.0)	27 (16.7)
Percent body fat[a]	33.9 (6.6)
Dietary	
PrimeScreen diet score[b]	18.2 (8.3)
Total energy intake (kcal/kg/day)[c]	30.4 (8.0)

*Continuous variables with normal distribution presented as mean (SD).
Categorical variables presented as count (%).
[a]n = 160.
[b]n = 125.
[c]n = 161.

5.6 Appendix 6 - Comparison of daily step counts measured by pedometers and accelerometers in the BHIP study

We conducted a comparative analysis of step counts measured by pedometer (Accusplit, Pleasanton) and accelerometer (SenseWear® armband MF-SW; BodyMedia® Inc., Pittsburgh PA) in the BHIP randomized trial to determine if adherence to the exercise intervention of 10,000 steps per day is similarly quantitated. Daily pedometer step counts were collected for 7 days at bi-weekly visits throughout pregnancy and accelerometer counts were measured over 3 days in the 2nd and 3rd trimester. Step counts from the pedometer and accelerometer were compared by paired t-test (IBM SPSS Statistics, Version 24.0.) and data was analyzed for 49 subjects of mean±SD age = 31 ± 3.7 yr; BMI = 25.3 ± 4.9kg/m^2. In the 2nd trimester, step counts were lower by accelerometer compared to pedometer counts collected two weeks prior (Figure 1) and two weeks after (Figure 2). In the 3rd trimester, step counts by accelerometer were also significantly lower than by pedometer collected two weeks prior (Figure 3). In summary, pedometers and accelerometers yield significantly different step counts in pregnant women, with pedometers giving a 1800-2000 higher reading. While pedometers may serve as motivational tools, accurate measures of physical activity level should be conducted using accelerometers. Compliance in wearing the devices declined from early to late pregnancy; continued compliance in pregnancy was observed in 81% of women for the pedometer and 92% for the accelerometer. Use of either device poses some challenges for women in late pregnancy, likely due to discomfort of the device, especially the pedometer which is worn on the hip.

Figure 1: Comparison of mean (SD) step counts by accelerometer in the 2nd trimester with pedometer two weeks before (n=42)

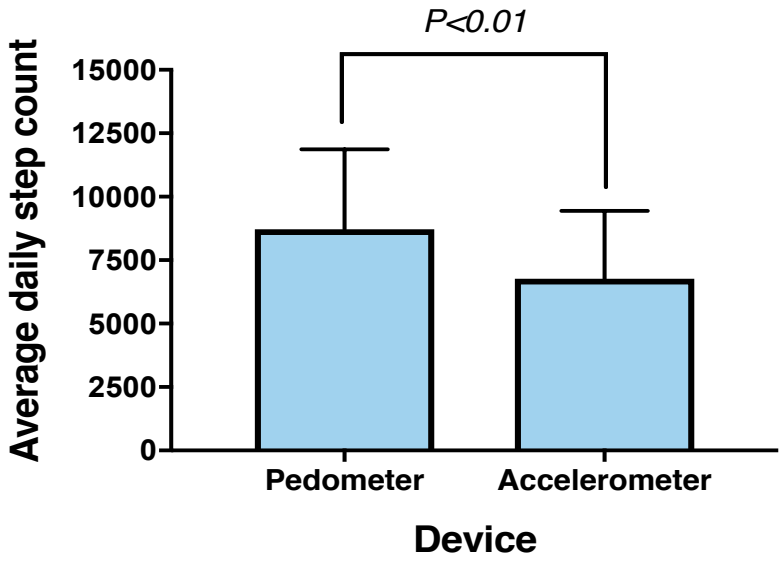


Figure 2: Comparison of mean (SD) step counts by accelerometer in the 2nd trimester with pedometer two weeks later (n=39)

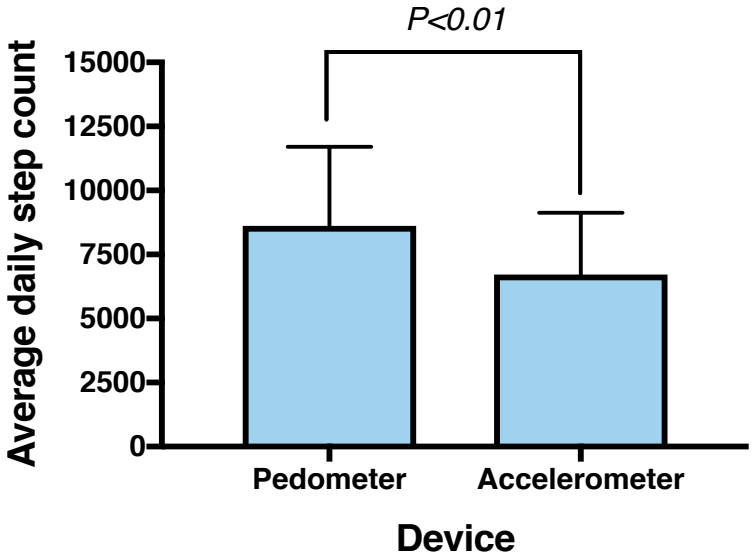
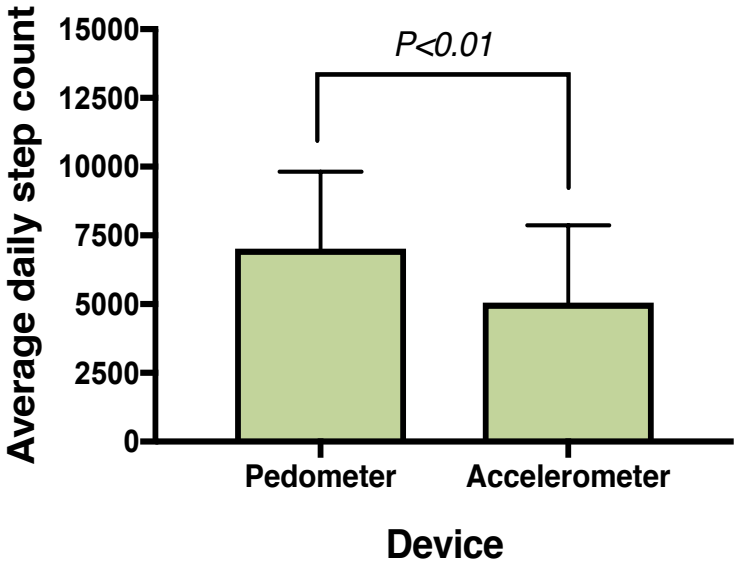


Figure 3: Comparison of mean (SD) step counts by accelerometer in the 3rd trimester with pedometer two weeks before (n=31)



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