DISCERNING THE INFLUENCE OF TOTAL BODY WEIGHT AND PREGNANCY ON THE CONTRIBUTION TO HEAT BALANCE

SHEILA DERVIS

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School of Human Kinetics
Faculty of Health Science
University of Ottawa

DEDICATION

To those who have thrived in the face of toxicity and negativity, I dedicate this to you. Seek help, encouragement, and a supportive environment. Keep pushing forward, do not let the actions of others dictate your future.

I also dedicate this thesis to my family, Rubie, Dan and Ellis. They are everything to me.

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PREFACE TO THIS THESIS

Following a surge of Covid-19 related cases of viral infections, we found ourselves amid a global pandemic early in year 2020. In March 2020, the province of Ontario declared a state of emergency, closing schools, all recreation programs, libraries, daycares, faith settings, bars/restaurants, and various other businesses. All Canadians were, and are still advised to maintain social/physical distancing practices as the state of emergency continues.

Unfortunately, this unprecedented pandemic put a stop to all data collection for researchers. During this time, my doctoral projects were well on their way, and we were about to start data collection for the last few lab-based experiments. I had received approval from my thesis advisory committee to present my thesis proposal, and my ethics submission was pending final approval. However, given the state of emergency and COVID-19 restrictions, I was unable to recruit and test new human participants as part of my PhD thesis projects. Considering I was entering my 7th year of the Doctoral program here at the University of Ottawa (due to changes in supervisor and thesis advisory committee) in September 2020, it was imperative to complete my studies as soon as possible. My current supervisor (Dr. Kristi Adamo) and thesis advisory committee members (Drs. François Haman and Carla Geurts) all supported the appropriate modifications of my thesis projects allowing me to complete my studies in a timely manner. Fortunately, the focus of the projects still includes thermoregulation across pregnancy. Although many of the measurements I intended to take were not possible, based on various decisions regarding acceptability, all changes meet the requirements of doctoral studies here at the University of Ottawa.

This thesis contains data collected as part of the large PhysicaL ACtivity and dietary implicatioNs Throughout pregnAncy (PLACENTA) study. I was able to contribute to the collection of the physiological and exercise testing data. The PLACENTA study was funded by

CIHR (MOP-142298), awarded to Dr. Kristi Adamo. Ethical approval was obtained from several Research Ethics Boards, including: the Ottawa Health Science Network (Protocol #20160178-01H), the Children's Hospital of Eastern Ontario (REB# 16/68X), Hôpital Montfort (#LG-01-06-16), University of Ottawa (#H11-15-29), Queensway Carleton Hospital (File# 17-03). The work contained in this thesis is my own, and I take full responsibility for its content.

I, Sheila Dervis, would like to express my gratitude to my supervisory and thesis advisory committee members for their support in continuing my doctoral projects amidst this unprecedented and uncertain time.

THESIS ABSTRACT

Evidence-based Canadian physical activity guidelines established specifically for pregnant women have shown to improve maternal and fetal outcomes, including prevention of adversities such as excess gestational weight gain, preeclampsia, and gestational diabetes. Unfortunately, most pregnant women fail to meet recommended guidelines for physical activity, and in many circumstances, the prevailing motive is due to a fear of overexertion and overheating harming the fetus. These concerns stem from reports of teratogenesis related to hyperthermia in several animal studies resulting in congenital fetal malformations. Although, due to disparities in thermoregulation between humans and animals, the findings are not entirely applicable to pregnant women. During exercise, the heat produced requires a given source of heat loss (i.e., skin blood flow/sweating) to maintain thermal homeostasis and a stable core temperature, preventing a continual rise in core temperature (i.e., teratogenesis). This thesis aims to separate the influence of pregnancy and body weight on oxygen consumption, heat production, heart rate, and rating of perceived exertion at rest (*Study 1)* and then during exercise (*Study 2)*. On the other side of the heat balance equation is heat loss mechanisms; currently, the limited existing literature suggests that dry and evaporative heat loss increases as pregnancy progresses. Unfortunately, these findings are also based almost exclusively on animal studies. There has not been an established understanding of physiological, perceptual/behavioural responses in heat loss in pregnant women from early to late pregnancy, and the final study in this thesis sought to map the current literature in the format of a scoping review (*Study 3*). The findings of this thesis provide evidence that physiological measurements of oxygen consumption, heat production and heart rate are not influenced by stage of pregnancy, the responses increases/decrease according to total body mass. Additionally, both dry and evaporative heat loss responses appear to increase from early to late pregnancy.

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LIST OF ABBREVIATIONS

ACOG American College of Obstetricians and Gynecologists

BMI Body mass index

CSEP Canadian Society of Exercise Physiology

GWG Gestational weight gain

IOM Institute of Medicine

H_{prod}/(M-W) Heat production/Metabolic heat production

NWM Non-weight matched

PA Physical activity

RMR Resting metabolic rate

SOGC Society of Obstetricians and Gynecologists of Canada

T1 Early Pregnancy 1, between 12 – 16 week gestation

T2 Middle Pregnancy 2, between 24 – 28 week gestation

T3 Late Pregnancy 3, between 34 – 38 week gestation

VCO_2 Carbon dioxide production

VO_2 Oxygen consumption

VO_2 Peak oxygen consumption

W_{ext} External work

WM weight-matched

CHAPTER 1: INTRODUCTION

1.1 Introduction & Background

Traditionally women were encouraged to reduce their workload throughout pregnancy and were counseled against engaging in physical activity (PA), allegedly to diminish adverse pregnancy outcomes. On the contrary, research advancements have shown that a physically active lifestyle during gestation results in numerous advantages, including better management of gestational weight gain (GWG), and lowering the risk of adverse health outcomes such as gestational diabetes (Ferraro *et al.*, 2012a; Nascimento *et al.*, 2012; Johnson *et al.*, 2013a; Ferraro *et al.*, 2015; Medek *et al.*, 2016; Lemmens *et al.*, 2018). In support of these outcomes, the Society of Obstetricians and Gynaecologists of Canada (SOGC), and the Canadian Society for Exercise Physiology (CSEP) jointly developed evidence-based PA guidelines for pregnant women (Davenport *et al.*, 2018a; Mottola *et al.*, 2018b). These joint physical activity guidelines recommend all women with healthy pregnancies partake in aerobic and strength conditioning exercises throughout gestation (Davenport *et al.*, 2018a; Mottola *et al.*, 2018b). The recommendations include a weekly accumulation of 150 minutes of moderate-intensity aerobic and strength conditioning exercises throughout pregnancy to maintain health benefits and reduce the risk of pregnancy-related complications (Davenport *et al.*, 2018a; Mottola *et al.*, 2018b).

Regardless of the evidence supporting PA throughout gestation, the majority of pregnant women fail to meet these recommendations, (Evenson & Wen, 2011; Santo *et al.*, 2017). Several reports indicate that a key motive as to why they choose not to engage in physical activity stems from a fear of overexertion and overheating (Franklin *et al.*, 2017a). Teratogenesis (i.e., processes that cause birth defects and/or malformations to an embryo or fetus) associated with hyperthermia has drawn considerable attention since several animal studies have linked it to congenital fetal malformations (Edwards, 1968, 1969; Edwards *et al.*, 2003). However, the results are not entirely applicable to humans because the physiological range in absolute temperature is much higher in animal studies compared to humans. Nonetheless, many reports on human subjects demonstrate that an increased core temperature induced by exercise and adverse environmental conditions may cause detrimental and even fatal consequences to non-pregnant and pregnant individuals (Edwards *et al.*, 2003; Ravanelli *et al.*, 2019). Maternal hyperthermia is considered a cause of teratogenesis during early gestation and remains a risk throughout late gestation (Edwards *et al.*, 2003). Heat generated from exercise (metabolic heat production) and/or hot ambient temperatures (environmental heat load) requires a given source of heat loss (i.e., skin blood flow/sweating) to maintain thermal homeostasis and a stable core temperature, avoiding a continual rise in core temperature (Wenger, 1972; Gagge & Gonzales, 1996; Jessen, 1996). The maintenance of core body temperature is a vital aspect of human survival, and, at rest, it is regulated at about 37°C.

Body weight has been shown to influence core temperature response to a given heat stress, such that as individuals gain weight (e.g., pregnant women) they will have a lower increase in core temperature due to a larger heat sink and potential to dissipate heat by virtue of increased body surface area compared to individuals with less body mass (e.g., non-pregnant women) (Havenith & van Middendorp, 1990; Cramer & Jay, 2016). Furthermore, since pregnant women with the same pre-pregnancy body mass as non-pregnant controls are heavier, they usually have a higher oxygen consumption (VO_2) for a given weight-bearing task. The rate of heat production is determined by the rate of absolute oxygen consumption (VO_2 in L/min), and when prescribed the same absolute heat production, the rate of increase in core temperature depends on total body weight (Cramer & Jay, 2016). Therefore, theoretically, exercise prescription based on a fixed heat production should result in smaller rises in core temperature across pregnancy due to the progressive nature of gestational weight gain (i.e., expanding heat sink). Several studies have shown that pregnant women compared to their non-pregnant controls have higher metabolic rates and heat productions during weight-bearing exercise, which is a reasonable response considering they are generally carrying more weight (i.e., gestational weight gain) for a given activity (Clapp *et al.*, 1987; Clapp, 1991; Morris & Johnson, 2005; Soultanakis, 2016). However, despite a higher heat load in pregnant women during exercise or passive heat exposure, several studies have shown that core temperature responses at rest (baseline) and during exercise are lower in pregnant women compared to their non-pregnant controls, suggesting a thermal feto-maternal protective mechanism (Clapp *et al.*, 1987; Clapp, 1991; Morris & Johnson, 2005; Soultanakis, 2016). Based on current literature a confounding variable that influences the physiological responses of metabolic rate and thermoregulation is body weight and due to the progressive increase in weight from early to late pregnancy it was not accounted for during exercise (Clapp *et al.*, 1987; Lof *et al.*, 2005; Lof & Forsum, 2006; DiNallo *et al.*, 2008).

A growing body of evidence demonstrates that physiological changes that occur during pregnancy are key modulators of the body's capacity to dissipate heat, favourably maintaining heat balance (Clapp *et al.*, 1987; Clapp, 1991; McMurray *et al.*, 1993; Hartmann & Bung, 1999; Hartgill *et al.*, 2011; Soultanakis, 2016; Ravanelli *et al.*, 2019). Notably, the shift in cardiovascular function, including increases in blood volume, stroke volume, cardiac output, heart rate, and decrease in systemic vascular resistance, contribute to enhanced dry heat loss mechanisms in pregnancy (Metcalfe & Ueland, 1974; Tan & Tan, 2013). Plasma and blood volume slowly increase by 40-50% throughout pregnancy to accommodate a growing and developing fetus, resulting in an increase in heart rate (15 beats/min more than usual), stroke volume, and cardiac output (Wenger, 1972; Soultanakis, 2016). Systemic vascular resistance also drops due to smooth muscle relaxation and overall vasodilation caused by elevated progesterone, leading to a fall in blood pressure (Wenger, 1972). Increases in blood flow appear to counteract the elevation of heat storage via dry heat loss (i.e., greater heat loss via skin blood flow and skin temperature) (Wenger, 1972; Evenson *et al.*, 2014; Cramer & Jay, 2016; Soultanakis, 2016). These processes are essentially transporting a greater amount of comparatively cooler blood from the periphery to the core and lowering body temperature. Any deficiencies in heat exchange from fetus – to mother - to the environment could result in maternal core temperature elevations, thus increasing risks of teratogenesis (Clapp *et al.*, 1987; Evenson *et al.*, 2014; Mottola *et al.*, 2018b). Fetal temperature depends on maternal temperature, fetal metabolic rate, and uterine blood flow, with the major effect being exerted by maternal temperature (Jessen, 1996; Ravanelli *et al.*, 2019).

An increase in blood volume associated with the growth of the feto-placental unit creates a mechanism that improves the efficiency of heat dissipation during pregnancy and helps maintain optimal feto-maternal heat transfer and dissipation (Schröder & Power, 1997). A recent systematic review suggests that pregnant women can safely participate in up to 35 minutes of very high-intensity aerobic exercise (~90%HRmax) at an air temperature of 25°C and 45% relative humidity without reaching a core temperature of 39.0°C (Ravanelli *et al.*, 2019); which has been considered a teratogenic threshold during pregnancy (Graham *et al.*, 1998; Miller *et al.*, 2002; Soultanakis, 2016). Although the thermoregulatory related maternal-fetal protective responses exist and maternal exercise is associated with improved health outcomes for both mother and offspring, there are still concerns of teratogenic consequences from exercise, and particularly, exercise in warm temperatures.

Throughout pregnancy, one of the most apparent changes that occurs is weight gain. During weight-bearing exercise, body weight greatly influences heat production (Most *et al.*, 2019b). Disparate results exist in metabolic rate in various reports when comparing stages of pregnancy and exercise (Clapp *et al.*, 1987; Lof *et al.*, 2005; Lof & Forsum, 2006; DiNallo *et al.*, 2008). Accordingly, it would be valuable to examine the influence of pregnancy separate from body weight on metabolic heat production. An important factor to be elucidated is whether there is a maternal-fetal protective response linked to heat production. To date, there has not been any research focusing on the independent influence of body weight and pregnancy on heat production at rest and during exercise. The complete thermoregulatory responses across pregnancy must also consider the other side of the heat balance equation, heat loss. Existing literature suggests that the cardiovascular shift associated with pregnancy may affect heat loss responses, including sweating and skin blood flow (Ginsburg & Duncan, 1967; Myhrman *et al.*, 1980; Clapp, 1991; McMurray *et al.*, 1993).

1.2 Objectives & General Hypothesis

The objective of this thesis was to explore metabolic rate changes and heat loss responses across pregnancy timepoints in healthy women with uncomplicated pregnancies. This objective has three specific aims:

1. To characterize resting metabolic rate and heat productions from early (T1), middle (T2) and late (T3) pregnancy timepoints.
2. To separate heat production responses during exercise into two groups in a cross-sectional inter-individual design: a) matching body weight of participants at early (T1), middle (T2) and late (T3) timepoints of pregnancy and b) not matching participants

body weight between pregnancy timepoints. Each timepoint of pregnancy (i.e., T1, T2, and T3) represents a different individual participant.

3. To explore current literature on heat loss mechanisms including, sweating, skin blood flow, skin temperature, other dry heat loss avenues and behavioural/perceptual responses across pregnancy.

These objectives will be tackled through three specific studies. The first objective will be addressed in STUDY 1 by measuring seated resting oxygen consumption and calculate heat production based on the phase of pregnancy and body mass. STUDY 2 will focus on the second objective by measuring heat production throughout a graded walking exercise test. The responses of heat production are compared based on pregnancy timepoint (early- T1, mid- T2, late- T3) and matching total body mass for each timepoint in pregnancy. Therefore, separating the influence of pregnancy timepoint and total body weight on the influence of heat production. The third objective will be undertaken in STUDY 3, by completing a scoping review on physiological and behavioural/perceptual heat loss responses in women across pregnancy.

Hypothesis

Based on our work and that of others, it was hypothesized that the effect of total body weight on heat production from resting to exercise would be independent of pregnancy timepoint (i.e., early, middle, and late stages of pregnancy). Therefore, as body weight increases (e.g., gestational weight gain in pregnancy), heat production will increase in parallel, indicating that total body weight modulates heat production at rest and during exercise.

1.3 Relevance of the studies and limitations

The results provided from this thesis may demonstrate the independent influence of total body weight (kg) and pregnancy time-point (T1, T2 and T3) on heat production at rest and during exercise. Furthermore, on the other side of the heat balance equation, the scoping review outcomes will provide current knowledge on physiological and perceptual/behavioural heat loss responses in women throughout pregnancy. Ultimately, the results may have practical implications for advancing physical activity guidelines for pregnant women as it pertains to heat-related risks and injuries. It must be noted that we are focused on healthy pregnancies (i.e., participants that meet the inclusion criteria of STUDY 1 and STUDY 2). Therefore, the results of these studies will not apply to women with metabolic disorders or cardiovascular issues.

CHAPTER 2: LITERATURE REVIEW

PREAMBLE OF LITERATURE REVIEW

This chapter contains a detailed literature review summarizing the current evidence assessing physiological and anatomical changes related to pregnancy and maternal exercise. More specifically, the review focuses on understanding human heat balance and how pregnancy influences thermoregulatory processes. To supplement the understanding of thermoregulation in pregnancy, this review contains parameters that influence subjective perceptual responses to heat stress (i.e., thermal sensation/comfort scale) and behavioural responses including sociodemographic factors and cultural/religious beliefs.

2.1 Physiological and Anatomical Changes Across Pregnancy

Throughout the entire nine months of pregnancy, a woman's body undergoes crucial physiological and anatomical s changes in response to fetal development. All body systems work jointly to provide an optimal environment for the fetus throughout pregnancy.

Anatomical/Musculoskeletal System

Gestational weight gain (GWG) is an expected and apparent morphological change that occurs throughout pregnancy. The majority of GWG occurs in the second and third trimesters of pregnancy (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009). Approximately 35% of expected pregnancy weight gain is accounted for by the placenta, fetus, and amniotic fluid (Pitkin, 1976). The remaining comes from increased blood volume/fluids, breast tissue, uterus, and fat stores. Maternal body weight represents a proxy marker of the mother's general health and that of the developing fetus. There is a sensitive balance in GWG; excessive and/or insufficient weight gain have been associated with adverse pregnancy outcomes, including large for gestational age (LGA) and small for gestational age (SGA) newborns, macrosomia, gestational diabetes mellitus (GDM), preeclampsia, postpartum weight retention, and downstream obesity for the child (Goldstein *et al.*, 2017). Health Canada employs the U.S. Institute of Medicine 2009 (IOM) (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) recommendations when advising women about gaining weight as part of a healthy pregnancy. The IOM guidelines suggest a different range of weight gain for each pre-pregnancy BMI category (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009).These guidelines provide practical, specialized weekly (kg/week) and absolute (total kg) weight gain recommendations based on a woman's pre-gravid BMI (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009; Ferraro *et al.*, 2012a; Ferraro *et al.*, 2015).

In a healthy pregnancy, women frequently face musculoskeletal issues as their morphology adjusts for a developing fetus. The centre of gravity persistently moves higher with increasing GWG. Muscular and ligament strain surrounding the vertebral column increases, which commonly results in low back pain of varying severity (Hartmann & Bung, 1999). As pregnancy progresses, the uterus expands into the abdominal cavity and displaces the maternal centre of gravity resulting in continuous lumbar lordosis and rotation of the pelvis on the femur. To compensate, the center of gravity shifts back to prevent the woman from falling forward. Furthermore, endocrine changes, including greater estrogen and relaxin levels related to pregnancy, increases the synovial fluid that facilitates laxity/widening in joints and ligaments. Despite the evident benefits of this during delivery, this augmented elasticity and flexibility in joint mobility can be a source of injury, especially during weight-bearing physical activity (Hartmann & Bung, 1999). Around the third trimester of pregnancy, despite a more significant laxity of ligaments, there is diminished flexibility in hand/foot joints due to increased water retention. Altogether, the morphometric adjustments, such as weight gain, a shift in the centre of gravity, and reduced joint stability, present challenges in safe/efficient motor coordination during pregnancy (Hartmann & Bung, 1999). Despite some of the morphometric transformations, women are encouraged to meet physical activity guidelines throughout pregnancy, in fact, all clinical guidelines support the notion that moderate-intensity physical activity can be safely performed across pregnancy (Mottola *et al.*, 2018a). Our group's recent finding of unchanged mechanical efficiency across gestation further supports the idea that moderate-intensity physical activity can be safely performed in pregnancy (Denize *et al.*, 2019).

Respiratory System & Energy Expenditure

An expanding uterus and increasing abdominal pressure elevates the diaphragm by approximately 4 cm and expands the chest circumference by about 5 to 7 cm throughout pregnancy. The respiratory adjustments extend to ventilation, which increases about 30%. The volume of air remaining in the lungs upon normal resting exhalation (i.e., functional residual capacity) reduces by 10 to 25% during pregnancy (Tan & Tan, 2013). The combined respiratory adjustments associated with GWG during pregnancy largely contribute to ventilator changes and resting metabolic rate (RMR). Inspiratory capacity increases, and that elevates the rate of oxygen consumption resulting in a higher RMR.

Total daily energy expenditure (TDEE) is the sum of energy expended to support RMR. The RMR accounts for approximately 60 to 80% of TDEE and depends on body mass, sex, age, and ethnicity. Moreover, approximately 60 to 70% increase in RMR during pregnancy is attributed to GWG (Butte *et al.*, 1999; Butte *et al.*, 2004; Lof & Forsum, 2006; Melzer *et al.*, 2010; Byrne *et al.*, 2011; Gilmore *et al.*, 2016). Energy intake requirements in pregnancy are those necessary to support optimal maternal tissue and fetal development (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009; Most *et al.*, 2019b). Throughout pregnancy, energy requirements are aimed at appropriate weight gain to best support fetal growth, maternal tissues such as fat mass, breast tissue, expanding uterus, and the placenta (Most *et al.*, 2019c). Accordingly, the 2009 IOM weight gain recommendations are inversely proportional to maternal BMI (kg/m^2) prior to pregnancy (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009). As shown in Table 1, women of a normal BMI (18.5 to 24.9 kg/m^2) the recommended weight gain during pregnancy is 11.5 to 16.0 kg, this range is increased for those underweight (<18.5 kg/m^2) and decreased for those overweight (> 24.9

kg/m^2)/obese (> 30 kg/m^2) (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009).

Table 1. Institute of Medicine Guidelines for gestational weight gain, by pre-pregnancy BMI.

Pre-Pregnancy BMI	Total Weight Gain (kg)	Rate of Weight Gain in 2nd and 3rd Trimesters of Pregnancy (kg/week)
Underweight (<18.5 kg/m2)	12.5-18	0.44-0.58
Normal Weight (19.5-24.9 kg/m^2)	11.5-16	0.35-0.50
Overweight (25.0-29.9 kg/m2)	7-11.5	0.23-0.33
Obese, **all categories** (≥30 kg/m2)	5-9	0.17-0.27

Physical activity largely contributes to a healthy pregnancy, despite the increased physiological demands placed on the body (Ferraro *et al.*, 2015; Davenport *et al.*, 2018c; Ruchat *et al.*, 2018). As pregnancy progresses, women carry more weight, including metabolically active tissues (Moya *et al.*, 2014). In the context of weight-bearing activity, pregnant women are typically heavier than non-pregnant women, particularly in later stages of pregnancy. Given this additional weight, pregnant women will be working at a higher relative percentage of their aerobic capacity for a given intensity of work or physical activity. Given the morphometric adjustments (i.e., changes in centre of gravity), it has generally been assumed that the efficiency of walking throughout pregnancy is impaired. However, a recent study performed by our lab explored the walking mechanical efficiency across the entire gestational period in healthy women (Denize *et al.*, 2019). The outcomes of mechanical efficiency built on evidence reporting that women expend more energy to perform the same walking task from early to late pregnancy and did more external work for the given task (Huang & Kuo, 2014) The authors reported mechanical efficiency to be unaffected by pregnancy when comparing the same walking tasks across gestation—implying that despite the phase of pregnancy and the associated morphological differences, mechanical efficiency remained unaffected (Denize *et al.*, 2019). These findings suggest there are other physiological parameters (i.e., body weight) influencing energy expenditure during weight-bearing exercise.

Cardiovascular System in Pregnancy

The process of pregnancy is dynamic and includes substantial changes in the cardiovascular system. These changes ensure that uteroplacental circulation is sufficient for fetal growth and development. Accordingly, along with vasodilation of the systemic vasculature, there is an increase in stroke volume and maternal heart rate, contributing to the 30%–50% increase in cardiac output during pregnancy (San-Frutos *et al.*, 2011; Tan & Tan, 2013). There is a rise in cardiac output of 4.6 L/min to 8.7 L/min from non-pregnant to pregnant women (San-Frutos *et al.*, 2011; Tan & Tan, 2013). The blood flow to the uterus and placenta constitutes up to 25% of the cardiac output and is important for the development of the fetus (San-Frutos *et al.*, 2011; Tan & Tan, 2013). In addition, the blood flow to the skin, kidneys and mammary tissues also increases (San-Frutos *et al.*, 2011; Tan & Tan, 2013). Essentially the cardiovascular shift that occurs in pregnancy includes a decrease in systemic/peripheral vascular resistance and increase in distensibility and dilation of the vasculature (San-Frutos *et al.*, 2011; Tan & Tan, 2013). As pregnancy progresses, cardiac output increases in early and middle stages, then plateaus by the end of gestation, as a result, blood pressure is lowest in early and middle stages of pregnancy (San-Frutos *et al.*, 2011; Tan & Tan, 2013). The upregulated blood flow to the skin directly benefits maintaining heat balance throughout pregnancy (Ziskin & Morrissey, 2011).

A study that measured total hand blood flow by venous occlusion plethysmography in 14 healthy women, from early to late pregnancy, reported that mean hand blood flow increased progressively from 7.7, in the early stages of pregnancy, to 28.9 mL/100 mL/min at term (Myhrman *et al.*, 1980). The greater skin blood flow and, in turn, convective dry heat loss across pregnancy enables heat dissipation in pregnancy, particularly while exercising. The heat production from muscular contraction is initially transferred to surrounding tissue via the circulatory system, which eventually dissipates to the environment through the skin surface by dry heat loss (Abramson *et al.*, 1943; Ginsburg & Duncan, 1967; Vaha-Eskeli *et al.*, 1991; McMurray *et al.*, 1993; O'Neill, 1996).

2.2 Exercise During Pregnancy

Throughout pregnancy, physical activity can generate a potential hindrance in the maternal capacity to meet fetal needs by greater substrate utilization, excess by-product production, and heat generation. Despite perceived limitations of exercise, studies have shown exercise to be safe and quite beneficial for the developing fetus (Ferraro *et al.*, 2012b; Nascimento *et al.*, 2012; Medek *et al.*, 2016; Davenport *et al.*, 2018b; Lemmens *et al.*, 2018). Today's evidence-based physical activity guidelines recommend all healthy pregnant women partake in aerobic and strength conditioning exercises throughout pregnancy (Davenport *et al.*, 2018a; Mottola *et al.*, 2018a). These guidelines identified that 150 minutes of moderate-intensity activity per week provides health benefits and reduces the risk of pregnancy- related complications (Davenport *et al.*, 2018a; Mottola *et al.*, 2018a). In the absence of any medical or obstetrical contraindications, the SOGC/CSEP recommend that pregnant women engage in at least 30 minutes of daily moderate-intensity aerobic and strength conditioning exercise, during most or all days of the week (Mottola *et al.*, 2018b)

Previous studies have presented that, compared to sedentary pregnant women, those who are physically active indicate less musculoskeletal pain, depressive symptoms, GWG, and postpartum weight retention, urinary incontinence as well as gestational diabetes and insulin resistance (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009; Nascimento *et al.*, 2012; Johnson *et al.*, 2013b). In western societies, a crucial motivator for regular physical activity during pregnancy is minimizing excessive GWG and subsequent postpartum weight. Despite longstanding concerns about the potential danger of physical activity in pregnancy (Guelfi *et al.*, 2015), there is an increase in awareness among women regarding the advantages of maintaining regular physical activity throughout pregnancy. Not to mention greater promotion of physical activity as a beneficial habit throughout pregnancy.

Data from the Canadian Community Health Survey (2005 to 2008) demonstrated that the prevalence of women meeting Canadian guidelines for physical activity (Davies *et al.*, 2003a) during pregnancy was only 23.3% (Gaston & Vamos, 2013). A a 2017 review concluded that the top two c reasons for not meeting physical activity guidelines during pregnancy were: 1) personal and culturally driven factors, and/or 2) lack of obstetric provider knowledge and limited guidance for exercise given to their pregnant patients (Newton & May, 2017). Furthermore, pregnant women were less likely to be meeting the guidelines if they were separated/divorced, single or a visible minority (Gaston & Vamos, 2013), among several other factors, including cultural values (Ejidokun, 2000; Wulandari & Klinken Whelan, 2011; Ngongalah *et al.*, 2018), and physical or social environments (Basu *et al.*, 2010; Basu *et al.*, 2018) and perceived barriers such as overexertion/overheating (Cramp & Bray, 2009).

2.3 Human Heat Balance

The maintenance of core body temperature is a vital aspect of human survival. At rest, it is regulated at about 37°C for optimal physiological functioning, which is considered a normothermic/euthermic state. During increases in metabolic and/or environmental heat loads, thermal homeostasis is crucial to avoid continual increases in core temperature. Metabolic energy expenditure is the rate of energy released to resupply adenosine triphosphate (ATP) for cellular activities such as muscle contraction. During exercise, metabolic energy is converted into mechanical energy and released thermal energy (as heat). The difference in metabolic energy expenditure and external work is defined as metabolic heat production. Environmental heat loads may passively heat the body in conditions with ambient temperatures exceeding skin temperature. To maintain thermal homeostasis heat generated from exercise (metabolic heat production) and/or hot ambient temperatures (environmental heat load) requires a given source of heat loss (i.e., evaporative and dry heat loss) in order to help maintain a stable core temperature.

The following is a classic conceptual 'heat balance' equation (Gagge & Gonzales, 1996):

$S = M - (\pm W) \pm (R + C) - E$……………………W·m^{-2}……………………………………. (1)

Where: *S* is the rate of body heat storage;

M is the rate of metabolic energy expenditure;

W is the rate of external work which is positive if it is being performed against an external force, or negative for eccentric or negative work;

R is the rate of radiant heat exchange;

C is the rate of convective heat exchange and;

E is the rate of evaporative heat exchange.

This equation states that a rate of body heat storage (S) occurs if metabolic heat production (M-W), which is the difference between metabolic energy expenditure (M) and external work (W), is not balanced by the combined heat dissipation to the environment via conduction (K), convection (C), radiation (R) and evaporation (E). To attain heat balance, the rate of heat storage must equal zero. However, a positive heat storage (S) such that occurs during exposure to hot ambient conditions and/or exercise in the heat will result in an increase in core temperature (i.e., hyperthermia). In contrast, a negative (S) such that occurs during a cold exposure for an extended period will result in a decrease in core temperature (i.e., hypothermia).

Sensible heat loss (±K±C±R) follows the second law of thermodynamics that states heat flows from a higher to lower temperature until thermal equilibrium is attained. Each component is a potential source of heat gain (+) or loss (-) (Nishi, 1981). Conduction (±K) is the heat transfer rate between two solid objects in contact. In the present study, the heat transfer across a small conductive cross-sectional area from the recumbent chair to the skin surface will not sufficiently influence whole-body heat exchange. Therefore, conduction will be considered negligible.

Respiratory Heat Loss ($+C_{res}+E_{res}$) is the heat transfer occurring through the inhaled and exhaled air along the respiratory tract. Also, when air of a certain absolute humidity (P_a) is inhaled, it leads to evaporative heat loss through respiration. The most effective means of heat loss is through the evaporation of sweat (Wenger, 1972). Moisture present on the skin creates a vapour pressure difference between the skin's surface and surrounding air, enabling evaporation. Every gram of vaporized sweat, at a constant temperature, results in 2.426 kJ of energy dissipated to the environment (Wenger, 1972). A given environment can provide a maximal evaporative capacity (E_{max}) and, depending on the given heat load, there will be a particular requirement of evaporation (E_{req}) to maintain heat balance.

In most animal cells, adenosine-triphosphate (ATP) works as the main carrier of chemical energy. In general, the human body uses three types of substrates to yield the necessary energy to drive ATP production: lipids, carbohydrates, and proteins (El Bacha *et al.*, 2010). Depending on the demand of work a series of aerobic and anaerobic pathways synthesize ATP. The mitochondria are the main site for ATP production, although a small amount can be produced anaerobically in the cytoplasm. Metabolic energy (M) is generated from the use of oxygen and substrates, including carbohydrates, lipids and proteins, and is an inefficient process (e.g., when cycling only ~20% of metabolic energy produced is directed to external work, the rest is released as metabolic heat) with most energy released as heat, distributed in the bloodstream (Parsons, 2003). Therefore, heat is a by-product of metabolism, and an increase in external work will result in greater metabolic demand and thus metabolic heat produced. An estimate of metabolic rate can be made by measuring how much oxygen has been used for a given 'work'. This measurement is possible by collecting expired air. The caloric value depends on the proportions of carbohydrates, fats and protein in food ingested. A measure of carbon dioxide produced will provide a proportion of substrate utilized and is represented by the respiratory quotient. Indirect calorimetry is commonly used to calculate metabolic energy expenditure (M) by estimating the amount of oxygen used to convert substrates to make ATP, as shown in the equation below (Nishi, 1981):

$$M = VO_2 \cdot \left(\frac{RER - 0.7}{0.3} \cdot e_c + \frac{1 - RER}{0.3} \cdot e_f\right) \text{ ....kJ/min.................................. (2)}$$

Where volume of oxygen consumption (VO_2) is in $L \cdot min^{-1}$; RER is the respiratory exchange ratio of carbon dioxide and oxygen; e_c is the caloric energy equivalent per liter of oxygen for the oxidation of carbohydrates (21.13 kJ); e_f is the caloric energy equivalent per liter of oxygen for the oxidation of fat (19.62 kJ).

There are two physiological pathways that most effectively maintain thermal homeostasis; 1) evaporative heat loss; evaporation of sweat from the skin and 2) dry heat loss: skin blood flow/cutaneous vasodilation (Wenger, 1972). Physiological processes and individual characteristics (Notley *et al.*, 2017) such as pregnancy (Ravanelli *et al.*, 2019), ageing (Stapleton *et al.*, 2015a, b), sex differences (Gagnon & Kenny, 2012), fitness levels (Lamarche *et al.*, 2018) and chronic conditions (i.e., diabetes, hypertension, etc.) (Kenny *et al.*, 2013) contribute to variability in the mechanisms involved in sweating and skin blood flow responses for a given heat load. As such, a given heat load may place some individuals at a higher risk for heat-related injury than others.

2.4 Thermoregulation: Rest to Exercise

Changes in thermal sensation and comfort typically influence thermoregulatory behaviour response (Gagge *et al.*, 1969; Schlader *et al.*, 2011). Both thermal sensation and comfort are considered subjective scales. Thermal sensation provides information regarding the individual's conscious feeling of being warm or cold (Nakamura *et al.*, 2008). In comparison, thermal comfort is more of a state of mind that conveys satisfaction within a given environment (Nakamura *et al.*, 2008). Physiological parameters such as core and skin temperatures are closely related to the perceptual responses found in both thermal sensation and thermal comfort (Gagge *et al.*, 1969; Marks & Gonzalez, 1974; Wang *et al.*, 2007; Zhang *et al.*, 2010). For example, a study reported a correlation between finger temperature and thermal sensation perceptual responses (Wang *et al.*, 2007). In response to thermoregulatory behaviour the deviations in skin temperature may elicit a level of thermal discomfort that could trigger a change in behaviour to avoid further discomfort (Gagge *et al.*, 1969; Song *et al.*, 2012; Schlader *et al.*, 2013). Therefore, skin temperature may be a possible prediction of thermal behaviour.

There exist differences in perceptual responses in thermal sensation/comfort for a given ambient temperature between various populations. The most evident difference that has been reported is the comparison between males and females as it relates to scales in thermal sensation/comfort. Females have a greater sensitivity to changes in ambient temperature in that they have been reported to express more frequently changes in their thermal sensation/comfort scales, when compared to males in a given environmental condition (Cena & de Dear, 2001;

Karjalainen, 2012; Kingma *et al.*, 2012; Schellen *et al.*, 2012). Additionally, it seems that females are more sensitive than males to a deviation from a comfortable temperature (i.e., not hot or cold) (Pellerin & Candas, 2003). As such, when ambient environmental conditions change, females might demonstrate modifications in thermoregulatory behaviour sooner than their male counterparts. Therefore, females are an interesting subpopulation to examine considering the dramatic physiological transformations that occur across their life, including pregnancy and menopause (Jacquot *et al.*, 2014).

Processes of Heat Exchange

Throughout the human body there are peripheral thermoreceptors responsible for identifying changes in skin and core temperatures. There are both warm and cold thermoreceptors are present in the skin, maintaining a basal tonic activity in thermoneutral environments. In response to a given magnitude rise/decline in temperature, these skin receptors increase/decrease their firing rate to maintain a stable core temperature (Pierau, 1996). The primary central area responsible for controlling body temperature is the preoptic region of the anterior hypothalamus (PO/AH), where thermoregulatory signals are integrated to elicit appropriate thermo-effector responses (Hammel *et al.*, 1960). When the PO/AH receives sensory afferent information indicating that core temperature is above a set point, proportional increases in responses (i.e., skin vasodilation and sweating) promote heat loss. For example, when the rate of heat gain associated with an increase in metabolic and/or environmental heat load exceeds that of total heat loss, the resultant rise in core and/or skin temperatures will elicit heat loss responses such as cutaneous vasodilation and sweat rate (Hammel *et al.*, 1960; Hammel, 1968; Benzinger, 1969). These effector heat loss responses (i.e., sweating and cutaneous vasodilation) function to enable the body to attain and/or maintain heat balance (Kondo *et al.*, 1998).

An increase in both skin blood flow and sweating are associated with a temperature onset threshold (Bligh, 2006), and beyond it, the rate of increase (i.e., thermosensitivity) is proportional to the change in core and/or skin temperature (i.e., mean body temperature) (Fusco *et al.*, 1961; Hammel, 1968; Gagge & Gonzales, 1996). The contribution of changes in both core and skin temperature affects the sensitivity of heat loss responses (Fusco *et al.*, 1961; Nadel *et al.*, 1971; Jessen, 1996; Wissler, 2008). As such, the rate of increase in effector response is generally measured using a calculated weighted summation of core and mean skin temperature, known as mean body temperature. The rate at which sweating and skin blood flow increases in response to the changes in mean body temperature is known as thermosensitivity (Hammel, 1968; Gagge & Gonzales, 1996). The onset threshold, thermosensitivity and capacity are integral in evaluating heat loss responses. They are influenced by physiological (e.g., female sex hormones, level of dehydration) (Pivarnik *et al.*, 1992; Sawka *et al.*, 1996) and biophysical characteristics (e.g., ageing, sex differences, fitness levels, chronic conditions) (Inoue *et al.*, 2005; Kenny *et al.*, 2010; Stapleton *et al.*, 2015a; Lamarche *et al.*, 2018).

In *figure 1*, there are three curves to demonstrate normal (grey open circles), elevated (red-dashed lines), and reduced responses (blue-dashed lines) of mean body temperature and heat loss responses for a given heat load. The given onset threshold of a mean body temperature is conveyed by the number 1, the thermosensitivity is represented by the number 2, and the plateau of heat loss responses is illustrated by the number 3. The red dashed line is an example of an effector response (i.e., sweating and/or skin blood flow) with a lower threshold and higher thermosensitivity to a given heat load when compared to the black and blue lines. Whereas the blue dashed line represents an impaired response in threshold and lower thermosensitivity for the same given heat load. As shown in *figure 1*, after the onset threshold, which represents the mean body temperature that initiates heat loss responses, the thermosensitivity is the rate at which heat loss responses continue to rise proportionally with increases in mean body temperature. This proportional linear progression serves as the thermosensitivity of the response. Once heat loss responses attain a maximal value or reached a maximal capacity, as seen in the number 3, the responses plateau/stabilize despite increasing mean body temperature. The red dashed line indicates a higher maximal heat loss response for a given change in mean body temperature and vice versa for the blue dashed line. Understanding the interaction/influence of factors such as pregnancy, aging, menopause, and sex differences on the onset threshold, thermosensitivities and maximal heat loss capacities provides valuable information on the body's thermoregulatory function across different populations/groups. The onset threshold and sensitivity for a given mean temperature provide further understanding of the possible variable mechanisms involved that may alter sweating and skin blood flow responses (i.e., hormones, hydration level, etc.). For instance, lower local sweat rate at a given mean temperature could be due to an increased onset threshold for sweating, such that an inflection in sweating does not occur until a higher mean temperature is reached, a decrease in sensitivity or both combined. Various factors that may alter the threshold and/or sensitivity of local sweating and/or skin blood flow include acclimation, level of dehydration, exercise training and female reproductive hormones (Ejidokun, 2000; Stapleton *et al.*, 2015a; Notley *et al.*, 2017; Most *et al.*, 2019b).

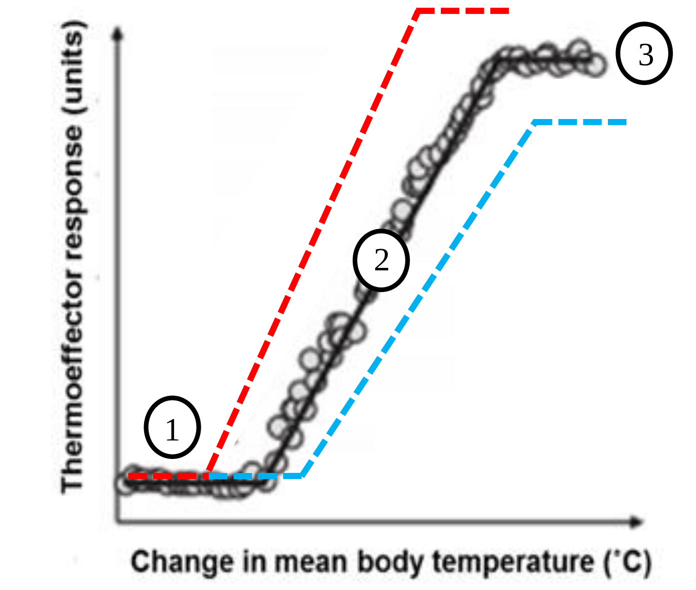

Figure 1. A schematic representation showing differences in onset threshold (1), thermosensitivity (2) and capacity (3) in heat loss responses (i.e., thermoeffector responses). The red dashed lines represent how variables can reduce onset threshold and increase both thermosensitivity and capacity of a given thermoeffector response (y-axis) at a given change in mean body temperature (x-axis). The blue dashed lines represent how variables can increase the onset threshold and decrease both thermosensitivity and capacity of a given thermoeffector response at a given change in mean body temperature. Adapted from Gagnon and Kenny, 2012.(Gagnon & Kenny, 2012)

Sweating and Skin Blood Flow Mechanisms

Human sweat glands are generally divided into two categories: the apocrine and eccrine glands. About 2 to 4 million eccrine sweat glands are distributed all over the skin and are primarily responsible for thermoregulatory sweating; these will be the ones referenced in this paper (Sato, 1977, 1993; Parsons, 2003). As core temperature increases, thermo-efferent stimulation (i.e., activation of heat loss responses) from autonomic nervous system via sympathetic cholinergic nerves release acetylcholine neurotransmitters at the sudomotor junction that bind to muscarinic receptors on the sweat glands, enabling sweat production (Randall & Kimura, 1955; Sato *et al.*, 1989). The rate at which acetylcholine can be broken down by acetylcholinesterase influences the rate of sweating (Hammel, 1968; Shibasaki *et al.*, 2006). The rate of sweating for a given heat load is determined by the density of heat-activated sweat glands and the overall rate/volume of sweat output per gland, which is controlled by a central integration of mean body temperature (Nadel *et al.*, 1971; Nadel *et al.*, 1974). The variability of the distribution of sweat glands that exists across the body (Weiner, 1945; Cotter *et al.*, 1995; Takano *et al.*, 1996; Kondo *et al.*, 1998) may be attributed to either the number of activated sweat glands and/or sweat output per gland (Sato & Dobson, 1970).

As a function of heat dissipation, sweating can only be as effective as the capacity to evaporate. Moisture present on the surface of the skin in the form of sweat creates a vapour pressure difference between the skin and the surrounding air; the larger the vapour pressure difference, the greater capacity for sweat to evaporate. The rate of evaporation of sweat from the surface of the skin has the highest potential for heat loss compared to other pathways (i.e., skin blood flow) at a given heat load because of its large latent heat of vaporization which is 2426 J per gram of sweat at 30°C (Wenger, 1972).

Core body temperature control at rest in a neutral environment is maintained primarily by skin blood flow (Brengelmann *et al.*, 1977). At rest, the rate of skin blood flow is about 250 mL/min, with increased heat load levels that can rise to approximately 6 to 8 L/min (Nagashima, 2006). The mechanistic function of cutaneous blood flow relies primarily on vasomotor tone that stems from vasoconstriction or dilation of peripheral blood vessels. Changes in skin blood flow in response to increases in heat load can derive from feedback from either the sympathetic vasoconstrictor system or the active vasodilatory system. During exercise and/or exposure to high environmental temperature more skin blood flow is accomplished by an increase in cardiac output and a redistribution of blood from the renal and splanchnic vascular beds to increase cutaneous vasodilation (Nagashima, 2006).

Cutaneous vasodilation can cause a several-fold influx in blood distribution to the surface of the skin, thereby increasing radiative, conductive, and convective heat transfer (and heat loss) from the core to the peripheral surface of the skin. Subsequently, heat loss via the evaporation of sweat, in turn, decreases skin temperature, thus cooling the blood from the dilated skin blood vessels that are returning to the core. Proportional to the rise in mean temperature, sweating, and skin blood flow will continue to increase until a steady state is attained or the point of maximum capacity (i.e., core temperature will continue to rise).

2.5 Biophysical changes in pregnancy and contributions to thermoregulation

The dynamic changes in weight composition during pregnancy to support the fetus as it develops are reflected by gestational weight gain, including maternal and fetal fat mass, fat-free mass, as well as placenta/amniotic fluid. The specific contributors to weight gain over the course of pregnancy are demonstrated in *Figure 2* (Pitkin, 1976; Widen & Gallagher, 2014). The resistance to heat transport from core to skin is formed by the body shell, consisting of muscle, adipose tissue, and skin. For a given thermal stress, vasodilation facilitates heat transfer from core to skin (Havenith, 2001). In conditions supporting vasoconstriction, heat flow from the core to the skin is primarily via conductance (Havenith, 2001). Additionally, body heat capacity, relevant for change in core temperature responses for a given thermal drive, depends on body mass and specific heat of tissues (Wyndham & Atkins, 1968). Specific heat of adipose tissue is 2.51 $J \cdot g^{-1} \cdot °C^{-1}$ and the combination of other tissues, including skin, skeleton, muscle etc., is on average 3.65 $J \cdot g^{-1} \cdot °C^{-1}$ (Wyndham & Atkins, 1968). Overall, biophysical characteristics, comprising height and weight ratios (i.e., body surface area) are acknowledged as essential factors mediating individual heat stress responses (Havenith, 2001). Considering the skin surface is in direct contact with the external environment; the combination of body height and weight (i.e., body surface area) has an important effect on whole-body heat exchange. Body surface area (BSA), defined as the area of the external surface of the body, is expressed in square meters (m^2) (Dubois & Dubois, 1916). In keeping with these concepts of BSA, from pre-pregnancy to the end of the third trimester, women change in weight and body morphology. In the context of changes in weight and morphology throughout pregnancy, women experience an increase in effective BSA (i.e., area of the skin in direct contact with the environment and able to contribute to heat dissipation). As pregnancy progresses, women will be able to maintain heat balance at a higher heat load (defined as the net heat gained of metabolic and environmental origin) compared to their smaller non-pregnant counterparts with lower effective BSA and therefore have a diminished ability to regulate body temperature. Moreover, in the contribution to heat exchange, body mass also has an important role as a thermal heat sink. For example, a given change in body heat content will result in an increase in core temperature, and a smaller individual with a lower body mass will experience a larger change in core temperature during exercise at a fixed absolute rate of heat production compared to a heavier individual (Hammel, 1968). Similarly, the heat loss potential considering body surface area, is greater among larger individuals with higher body surface areas. Since the achievement of heat balance depends on matching the rate of heat production with the same rate of heat loss, someone with a greater body surface area will be able to sustain a higher absolute rate of heat production while remaining in heat balance due to a greater heat loss potential (Havenith, 2001; Parsons, 2003; Cramer & Jay, 2016).

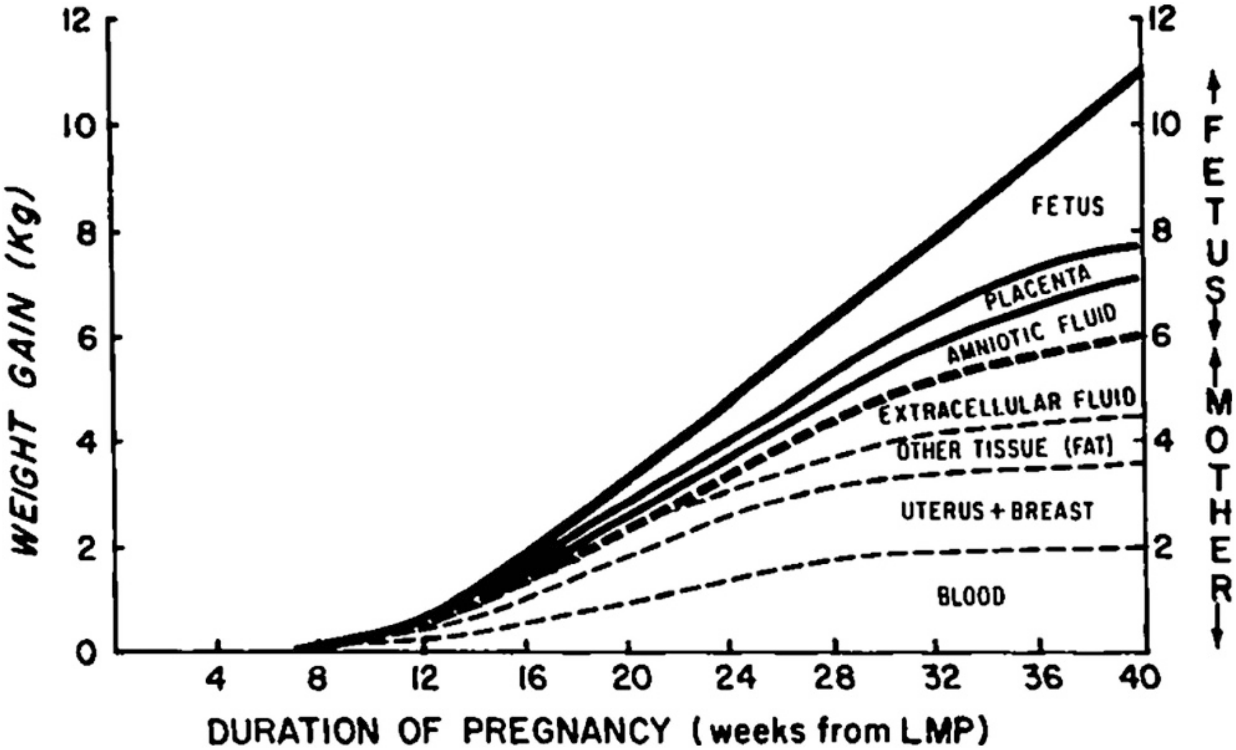

Figure 2. A reprinted pattern and average weight gain changes from early to late pregnancy, including maternal (blood, breast, other tissue (fat), extracellular fluid) and fetus (fetus, placenta and amniotic fluid) contributions. Source: Pitkin *et al* (Pitkin, 1976)

Peripheral thermoreceptors are responsible for identifying changes in skin and core temperatures. In response to a given degree rise/decline in temperature, these thermoreceptors increase/decrease their firing rate to maintain a stable core temperature (Boulant & Bignall, 1973; Wyss *et al.*, 1974; Romanovsky, 2007). It has been suggested that the increase in blood volume associated with the growth of the feto-placental unit creates a mechanism that improves the efficiency of heat dissipation during pregnancy and helps maintain optimal feto-maternal heat transfer, and thus dissipation to the environment (Schröder & Power, 1997). Increases or decreases in umbilical or uterine blood flow would increase or decrease, respectively, the rate at which the fetus loses heat through the placental route (Clapp, 1991; Hartgill *et al.*, 2011). The fetus produces large amounts of metabolic heat for its growth and development; this heat is transferred to the mother and is dissipated to the environment via placenta exchange through the umbilical cord (Hartgill *et al.*, 2011).

Several reports indicated that an increase in maternal core temperature could influence cell division in the embryo, resulting in neural tube defects and congenital alterations early in pregnancy (Graham *et al.*, 1998; Soultanakis, 2016). Although uncommon, maternal hyperthermia may cause teratogenesis during early gestation (Graham *et al.*, 1998; Miller *et al.*, 2002; Kukkonen-Harjula & Kauppinen, 2006) . Furthermore, chronic exposure to elevated heat late into gestation has been linked to growth restriction, possibly due to the heat-induced decrease in uteroplacental blood flow, which can cause placental insufficiency and a greater risk for elevated fetal temperature (Clapp *et al.*, 1987; Clapp, 1991; Morris & Johnson, 2005).

2.6 Rationale and statement of the problem

A recent systematic review by Ravanelli *et al.,* 2019 compared core temperature responses across pregnancy (from first to third trimesters) to non-pregnant controls (Ravanelli *et al.*, 2019). The authors (Ravanelli *et al.*, 2019) compared many studies with various exercise and environmental conditions, such as exercise in a warm bath (McMurray *et al.*, 1990; McMurray *et al.*, 1993) or resting exposure to a hot and dry sauna (Kukkonen-Harjula & Kauppinen, 2006) or immersion in a hot water bath (Tuffnell *et al.*, 2009). Ravanelli *et al.,* 2019 demonstrated that despite the large variety in heat loads measured (i.e., exercise and environmental), no published study has reported core temperature of a pregnant woman to exceed 38.0°C, 1.0 °C lower than the teratogenic threshold (Ravanelli *et al.*, 2019). Due to disparate findings, separating the influence of pregnancy timepoint (i.e., comparing early, middle, and late pregnancy) and total body weight on heat production during weight-bearing exercise would further clarify the contribution of weight and exercise intensity to heat production.

Certain ideal heat dissipation mechanisms, both physiological and perceptual/behavioural, may account for favourable core temperature responses during various heat stress conditions across pregnancy. For example, the aforementioned greater blood flow associated with cardiovascular adjustments throughout pregnancy is a physiological response that enables heat balance and maintains core temperature within a safe range (Schröder & Power, 1997). Moreover, several studies demonstrated a maternal-fetal protective response related to higher perceptual sensitivity to changes in ambient temperature. These studies identified that as pregnancy progressed, the sensitivity to changes in ambient temperature increased when compared to non-pregnant women (Clapp, 1991; Hartgill *et al.*, 2011). On the other side of the heat balance equation is heat loss. Currently, most findings on heat loss responses across pregnancy were gathered from animal studies (Curet *et al.*, 1976; Clapp, 1980; Chandler & Bell, 1981; Lotgering *et al.*, 1983; Power, 1989; Schröder & Power, 1994; Edwards *et al.*, 2003). Unfortunately, these results cannot be directly applied to humans due to differences in thermoregulatory thresholds (e.g., core temperature of sheep ~39°C, birds ~40-42 °C, and rats ~38.5°C) (Prozesky, 1963; Baker *et al.*, 1979; Edwards *et al.*, 2003) and heat loss mechanisms. Therefore, for a well-rounded understanding of heat balance mechanisms in pregnant women, it would be beneficial to consider the influence of heat production (accounting for weight) and heat loss responses (reviewing current literature of mechanisms already measured in pregnant women).

CHAPTER 3

PREAMBLE TO ARTICLE 1

This chapter sets the groundwork for discerning the influence of maternal and fetal weight gain throughout pregnancy on energy expenditure. For any given day, *most* of the energy expenditure falls within more or less sedentary limits, any changes in resting metabolic rate across pregnancy will play a major role in overall energy expenditure. Prior to investigating responses to exercise, we sought to separate the influence of healthy gestational weight gain and pregnancy timepoint on resting metabolic rate. The following study titled “Resting metabolic rate in weight-matched and non-weight matched women across pregnancy.” is presented in Chapter 3.

Title:

Resting metabolic rate in weight-matched and non-weight matched women across pregnancy.

Authors:

Sheila Dervis[a], Kristi Bree Adamo[a]

Author Affiliations:

[a] Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, Ottawa, ON, Canada, K1N 6N5.

Corresponding Author:

Dr. Kristi B. Adamo

Associate Professor

School of Human Kinetics, Faculty of Health Sciences

Lees Campus, E 250F

200 Lees Ave. Ottawa, ON K1N 6N5

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Conflict of Interest: None to disclose

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ABSTRACT

Background: The most significant influence on pregnant and non-pregnant women's energy requirements is total body weight. From early, middle, to late pregnancy, maternal and fetal weight changes as fetus grows. To assess pregnancy-related weight changes in resting energy expenditure, one must account for both total body weight and gestational weight gain. The purpose of this study was to compare resting oxygen consumption, heat production, and heart rate in weight-matched and non-weight matched pregnant women.

Methods: A 20-minute semi-reclined resting protocol was used to continually monitor oxygen consumption (L/min), heat production (kJ), and heart rate (bpm) in healthy, young women in early (T1), middle (T2), and late (T3) pregnancy. There were inter-individual comparisons made at the different pregnancy timepoints. Participants were separated into two groups: Group 1) all participants were matched for total body weight (WM) in early (T1), middle (T2) and late (T3) pregnancy and, Group 2) participants were not matched for total body (NWM) weight in T1, T2, and T3 timepoints of pregnancy.

Results: In the WM group, the experimental design elicited equivalent rates of heat production (kJ/min) in T1 (6.2 ± 2.9 kJ/min) compared to both, T2 (6.2 ± 2.1 kJ/min, $P = 0.98$) and T3 (6.8 ± 2.2 kJ/min, $P = 0.58$); heat production (kJ) in T1(125 ± 59 kJ) compared to both, T2 (124 ± 42 kJ, $P = 0.98$) and T3 (127 ± 32 kJ, $P = 0.91$); and heart rate (bpm) in T1 compared to both, T2 (75 ± 9 bpm, $P = 0.48$) and T3 (77 ± 9 bpm, $P = 0.15$) In the non-weight-matched groups (NWM), T3 demonstrated greater heat production (6.7 ± 2.0 kJ/min, $P = 0.044$), heat production (kJ) (133 ± 40 kJ, $P < 0.001$) and heart rate (81 ± 9 bpm, $P < 0.001$) compared to T1.

Conclusion: The current findings indicate that total body weight irrespective of timepoint in pregnancy significantly modulates physiological measurements of heat production, and heart rate during rest.

1.0 Introduction

In pregnancy, adequate energy requirements are associated with optimal health outcomes for both mother and fetus, avoiding gestational and perinatal morbidities (Carmichael *et al.*, 1997; Langford *et al.*, 2011). In 2009, the American Institute of Medicine (IOM) re-examined guidelines for weight gain based on the changes of women of childbearing years/obstetric populations (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009). These guidelines were developed to minimize the negative health consequences for both mother and fetus associated with inadequate or excessive gestational weight gain (Rasmussen *et al.*, 2009; Davies *et al.*, 2010). Pregnancy is an anticipated time for weight gain; two main contributors are energy intake and energy expenditure. During pregnancy, the energy requirements are calculated as the energy needed for maternal and fetal tissues, including the rise in the resting metabolic rate (RMR) (Butte *et al.*, 2004).

The calculations for energy expenditure in non-pregnant healthy women are primarily based on RMR and account for approximately 60-80% of the total daily energy expenditure (Melzer *et al.*, 2010; Most *et al.*, 2019b). Other variables included in total daily energy expenditure, such as diet-induced thermogenesis and level of physical activity, have been reported to be unaltered from non-pregnant to pregnant women, suggesting that most of the changes across pregnancy are due to RMR (Heini *et al.*, 1991; Spaaij *et al.*, 1994; Bronstein *et al.*, 1995; Piers *et al.*, 1995; Prentice *et al.*, 1996; Kopp-Hoolihan *et al.*, 1999; Butte *et al.*, 2004; Clarke *et al.*, 2005; Lof & Forsum, 2006; Rousham *et al.*, 2006; Melzer *et al.*, 2009). Several studies have reported an increase in RMR from early to late pregnancy and between pregnant and non-pregnant participants (Butte *et al.*, 2004; Byrne *et al.*, 2011; Gilmore *et al.*, 2016). The RMR has the greatest increase in the last trimester of pregnancy, with some studies reporting an approximate 20% or

200-400 kcal/day increase from non-pregnant women (Forsum *et al.*, 1992; Goldberg *et al.*, 1993; Prentice *et al.*, 1996; Kopp-Hoolihan *et al.*, 1999; Butte *et al.*, 2004; Lof *et al.*, 2005; Melzer *et al.*, 2009). One of the most consistent and greatest physiological/anatomical changes that occur during pregnancy is weight gain; in fact, several studies reported more than half of the increase in RMR is attributed to gestational weight gain (Butte *et al.*, 2004; Lof *et al.*, 2005; Melzer *et al.*, 2010; Byrne *et al.*, 2011; Gilmore *et al.*, 2016).

Our study aimed to assess the independent influence of total body weight on RMR, heat production and HR in early, middle, and late pregnancy. We sought to make these comparisons by matching participants for total body weight in early, middle, and late pregnancy. To date, several studies have indicated that weight largely determines energy expenditure, especially during rest (Forsum *et al.*, 1992; Goldberg *et al.*, 1993; Prentice *et al.*, 1996; Kopp-Hoolihan *et al.*, 1999; Butte *et al.*, 2004; Lof *et al.*, 2005; Melzer *et al.*, 2009). A recent review by Most *et al., 2019* consistently highlighted the importance of gestational weight gain on energy expenditure at rest and during exercise in general (Most *et al.*, 2019b). To our knowledge, this is the first study of its kind to assess total body weight separate from pregnancy timepoint and compare the inter-individual responses of participants in early, middle, and late pregnancy.

2.0 Methods

2.1 Ethical Approval

This study comprised a large data pool provided by CIHR-funded trial, PhysicaL Activity and dietary implicatioNs Throughout pregnancy (PLACENTA) study (MOP-142298). Accordingly, the PLACENTA protocol was approved by numerous ethics boards across Ottawa: University of Ottawa (#H11-15-29), Ottawa Health Sciences Network (REB# 20160178-01H), Children's Hospital of Eastern Ontario (REB# 16/68X), Queensway Carleton Hospital (File# 17-03), and

Hôpital Montfort (#LG-01-06-16). As a result, the presented study was performed in accordance with the Declarartion of Helsinki. All participants provided written, informed consent prior to participation.

2.2 Study Participants

All pregnant participants were selected from those who identified interest in participating in the PhysicaL Activity and dietary implicatioNs Throughout pregnAncy (PLACENTA) study. Participants were recruited from regional Ottawa hospitals, midwifery centres as well as university campuses, and social media platforms. The inclusion criteria for the pregnant participants were: 18 to 40 years old, ability to communicate in either English or French, carrying a singleton fetus, having a BMI (pre-pregnancy) of normal or overweight (18.5-29.9 kg/m2) and having no contraindications to exercise. Conversely, exclusion criteria constituted the following: habitual consumption of alcohol/drugs/tobacco, pre-pregnancy diabetes, untreated thyroid disease, or hypertension.

This study used a cross-sectional inter-individual comparison of pregnant women based on matching and not matching total body weight between pregnancy timepoints (T1, T2 & T3), so there are six distinct groups. The participants were asked to arrive at the Lees campus of the University of Ottawa. The visits occurred either in the early stage of pregnancy; between weeks 12 and 16 (T1), during the middle stage of pregnancy: between weeks 24 and 28 (T2) and/or late in pregnancy; between weeks 34 and 38 of gestation (T3). The participants were asked to refrain from exercise 24 hours before the visit.

2.3 Anthropometric Measures

All participants were instructed to change into exercise clothes. A trained research personnel measured the participant's maternal height and body mass for each visit (T1, T2 and

T3). Height (cm) was measured using a stadiometer (HR-200 Wall-Mounted Height Rod, Tanita Corporation of America Inc., Illinois, USA) in duplicate and reported to the closest 0.1cm. Once participants removed their footwear, they were instructed to stand with their feet together, back of the heels, buttocks and upper back touching the wall. Their arms hanging at their sides and gaze straight ahead, participants were asked exhale, after which the headboard of the stadiometer was lowered until it touched the top of the head. Measurements were recorded after participants moved away from the stadiometer. Afterward, body mass (kg) was measured using an electronic scale (BWB-800 Doctors Scale, Tania Corporation of America Inc., Illinois, USA), barefoot. Once the scale was zeroed, participants were instructed to stand in the centre of the scale and remain still. Once the weight stabilized, body mass was recorded to the nearest 0.1kg. Gestational weight gain (GWG) was then calculated by the difference in measured T3 body mass and self-reported pre-pregnancy weight. According to the Institute of Medicine 2009 Guidelines for those with a normal BMI a healthy total weight gain in pregnancy is between 11.5 to 16.0 kg (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009).

2.4 Data Collection & Experimental Protocol

All laboratory visits occurred in the morning between 6h00 and 10h00, and after an 8-hour fast. Following anthropometric measurements were recorded, the participants were given a standardized snack consisting of juice (orange or cranberry flavour), a granola bar, and fruit (~ 370 kcals).

After the standardized snacks were consumed, participants were instrumented with a HR monitor belt (Polar V800, Polar Electro Canada) worn around the chest. Then, participants were fitted with a metabolic mask, where expired gases were pulled through a T-type, one-way, non-rebreathing valve (Series 2700 Large: Hans-Rudolph, Shawnee, KS). Once instrumented, participants sat in a semi-reclined phlebotomist chair for 20 minutes in a comfortable room temperature chamber. The appraiser ensured that participants were not feeling cool by providing a blanket to use to their discretion. Throughout the test, continual measurements of the participants' respiration and HR were monitored.

2.5 Metabolic Measurements

Prior to the start of the resting period, mass flow generator (FK500, Sable Systems International Inc, Las Vegas, NV USA) was set at 100 L/min, at standard temperature, pressure and dry (STPD) conditions. Throughout testing barometric pressure (P_B), and the composition of inspired (f_i) and expired (f_e) air were measured from a 250 mL/min subsample using a field metabolic system (Sable Systems International Inc., Las Vegas, USA). The flow rate (FR) was converted to STPD using the following gas laws:

FR = ($T_{standard} \cdot P_B$)/ ($T_{ambient} \cdot P_{standard}$); FR = [273K· ($P_B$ kpa – WVP kpa)]/ 296K·101.3kpa.

Rate of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were calculated using the following equations.

$$VO2\left(\frac{L}{min}\right) = Flow\ Rate\ \left(\frac{L}{min}\right), STPD \times (fiO_2 - feO_2)$$

$$VCO2\left(\frac{L}{min}\right) = Flow\ Rate\ \left(\frac{L}{min}\right), STPD \times (feCO_2 - fiCO_2)$$

Measurements were taken continuously throughout both rest and exercise/recovery protocols. The fiO_2 and $fiCO_2$ are inspired fractions of the measured gas in ambient air; and feO_2 and $feCO_2$ are expired fractions of the measured gas exiting the mouthpiece. All gases measured were corrected for the partial pressure of water (P_{H2O}).

Heat Production (H_{prod})

Heat production (H_{prod}) was calculated as the difference between metabolic energy expenditure (i.e., metabolic rate) and external work output; H_{prod} = Metabolic Energy Expenditure – Work Output, since during the resting period participants are not performing any external work it was set at '0'. Heat Production ($\dot{M}$) in kJ per minute, was calculated using the respiratory exchange ratio (RER = VCO_2/ VO_2) in the following equation (Nielsen & Davies, 1976):

$$\dot{M}\ (kJ/min) = \left[\dot{v}O_2\ \left(\frac{L}{min}\right) \times \left(\frac{RER-0.7}{0.3} \cdot e_c + \frac{1-RER}{0.3} \cdot e_f\right)\right]$$

Both VO_2 and VCO_2 values were based on STPD conditions. Volume of oxygen consumption (VO_2) is in $L\cdot min^{-1}$; RER is the respiratory exchange ratio of carbon dioxide and oxygen VCO_2/ VO_2; e_c is the caloric energy equivalent per liter of oxygen for the oxidation of carbohydrates (21.13 kJ per L of O_2 consumed); e_f is the caloric energy equivalent per liter of oxygen for the oxidation of fat (19.62 kJ L of O_2 consumed).

2.6 Statistical Analysis

All statistical analyses were completed using SPSS statistical software (Version 27.0 for Windows; IBM, Armonk, NY). Descriptive statistics were performed for participant characteristics include maternal age (years), height (cm), weight (kg), BMI (kg/m^2), gestational weight gain (kg), weeks of gestation (weeks), baby weight (kg) and placenta weight (kg). One-way analysis of variance (ANOVA) was used to compared T1, T2, and T3 in both experimental groups. When significant differences were observed, *post hoc* analysis was performed using Bonferroni correction. For all analyses, the significance was set at $p \leq 0.05$.

In this cross-sectional inter-individual design, H_{prod} (kJ & kJ/min) and HR (bpm) were compared across pregnancy timepoints (T1, T2 & T3) during rest period and analyzed separately between the two experimental groups: 1) weight-matched (WM) and 2) non-weight-matched (NWM). Comparisons of responses to rest period (duration of 20 minutes) across T1, T2, and T3 were analyzed using a two-way mixed ANOVA for repeated measures. Where appropriate, all p-values were adjusted for multiple comparisons using the Bonferroni correction. H_{prod} (kJ) and HR values were plotted as a function of rest period. H_{prod} (kJ/min) and HR were computed as the average of the last 1-minute in the rest period.

3.0 Results

As designed, the characteristics of this cross-sectional interindividual comparison for both weight-matched (WM), and non-weight-matched (NWM) women across early (T1), middle (T2), and late pregnancy (T3) were similar in age and height as described in Table 1. In the WM group, fourteen pregnant women in each pregnancy timepoint (T1, T2 and T3) were matched for body mass (kg), meaning the group body weight at each timepoint was the same. In the NWM group, we were able to test twenty-three participants in T1, fifty-three participants in T2 and thirty-three participants in the T3 group. In Table 2, there are specific weight-related characteristics that relate to only T3 in both WM and NWM groups. In the NWM group, we tested twenty-four participants and in WM group we included thirteen participants. The gestational weight gain, baby weight and placental weight were all similar between WM and NWM in T3.

Table 1. Participant characteristics for weight-matched and non-weight matched pregnant women.

	Pregnancy Timepoint					
	WM			NWM		
	T1	T2	T3	T1	T2	T3
Age (years)	32 ± 4	32 ± 3	33 ± 4	32 ± 3	32 ± 3	32 ± 3
Gestational age (months)	15.2 ± 0.7	26.8 ± 1.2	35.8 ± 1.6	15.8 ± 0.9	27.2 ± 1.6	36.1 ± 1.8
Height (metres)	1.68 ± 0.07	1.66 ± 0.05	1.64 ± 0.05	1.67 ± 0.08	1.68 ± 0.06	1.67 ± 0.06
Body mass (kg)	71.6 ± 8.1	71.7 ± 8.0	71.5 ± 7.6	65.4 ± 8.9	74.8 ± 9.7 *	79.9 ± 8.9 *
Body Surface Area (m^2)	1.81 ± 0.13	1.80 ± 0.11	1.78 ± 0.11	1.73 ± 0.15	1.84 ± 0.84*	1.89 ± 0.12 *

Values are presented as mean ± SD. Weight-Matched (WM), T1 = early pregnancy, n = 14; T2 = mid-pregnancy 2, n = 14; T3 = late pregnancy, n = 14. Non-Weight-Matched (NWM), T1, n = 23; T2, n = 53; T3, n = 33. *p < 0.05, significantly different from T1.

Table 2. Maternal-fetal weights of pregnant women in T3 for weight-matched and non-weight matched groups

	T3	
	WM	NWM
Pre-pregnancy BMI (kg/m^2)	21.5 ± 1.8	23.6 ± 2.4 *
Gestational Weight Gain (kg)	12.7 ± 3.8	13.2 ± 4.0
Baby Weight (kg)	3.28 ± 0.37	3.27 ± 0.39
Placenta weight (kg)	0.56 ± 0.08	0.58 ± 0.11

Values are presented as mean ± SD. Pre-pregnancy BMI, gestational weight gain, baby and placenta weight taken from participants in the T3 group of weight-matched (n = 13) and non-weight matched group (n = 24). *p < 0.05, significantly different from weight-matched group.

3.1 Resting metabolic rate (RMR)

Figure 1 presents resting metabolic rate (RMR) expressed as a sum of the entire resting period as a sum in H_{prod} (kJ) and a rate as H_{prod} (kJ/min) from early (T1), middle (T2) to late (T3) pregnancy in both WM and NWM groups. The H_{prod} (kJ) represents the sum of 20-minutes of rest, whereas H_{prod} (kJ/min) is a 1-minute average taken at the end of the 20-minute resting period.

In the WM group, where the total body mass from T1, T2, to T3, was similar at about 71.6 ± 7.7 kg, there was no main effect of pregnancy timepoint (P = 0.365) and H_{prod} was also similar in T1 (125 ± 59 kJ) compared to T2 (124 ± 42 kJ, P = 0.98) and T3 (127 ± 32 kJ, P = 0.91). Accordingly, the there was no main effect (P = 0.356) of pregnancy timepoint on H_{prod} (kJ/min) and values were similar in T1 (6.2 ± 2.9 kJ/min), T2 (6.2 ± 2.1 kJ/min, P = 0.98) and T3 (6.8 ± 2.2 kJ/min, P = 0.58). In the NWM group, total body weight increased from T1 (65.4 ± 8.9 kg), T2 (74.8 ± 9.7 kg), to T3 (79.9 ± 8.9 kg), there was a main effect of pregnancy timepoint (P < 0.03) for both H_{prod} in kJ and kJ/min. The H_{prod} increased from T1 (103 ± 34 kJ), T2 (126 ± 39 kJ, P = 0.02), to T3 (133 ± 40 kJ, P < 0.001) as did the H_{prod} (kJ/min) from T1 (5.5 ± 2.2 kJ/min), T2 (6.7 ± 2.3 kJ/min, P = 0.041), to T3 (6.7 ± 2.0 kJ/min, P = 0.044).

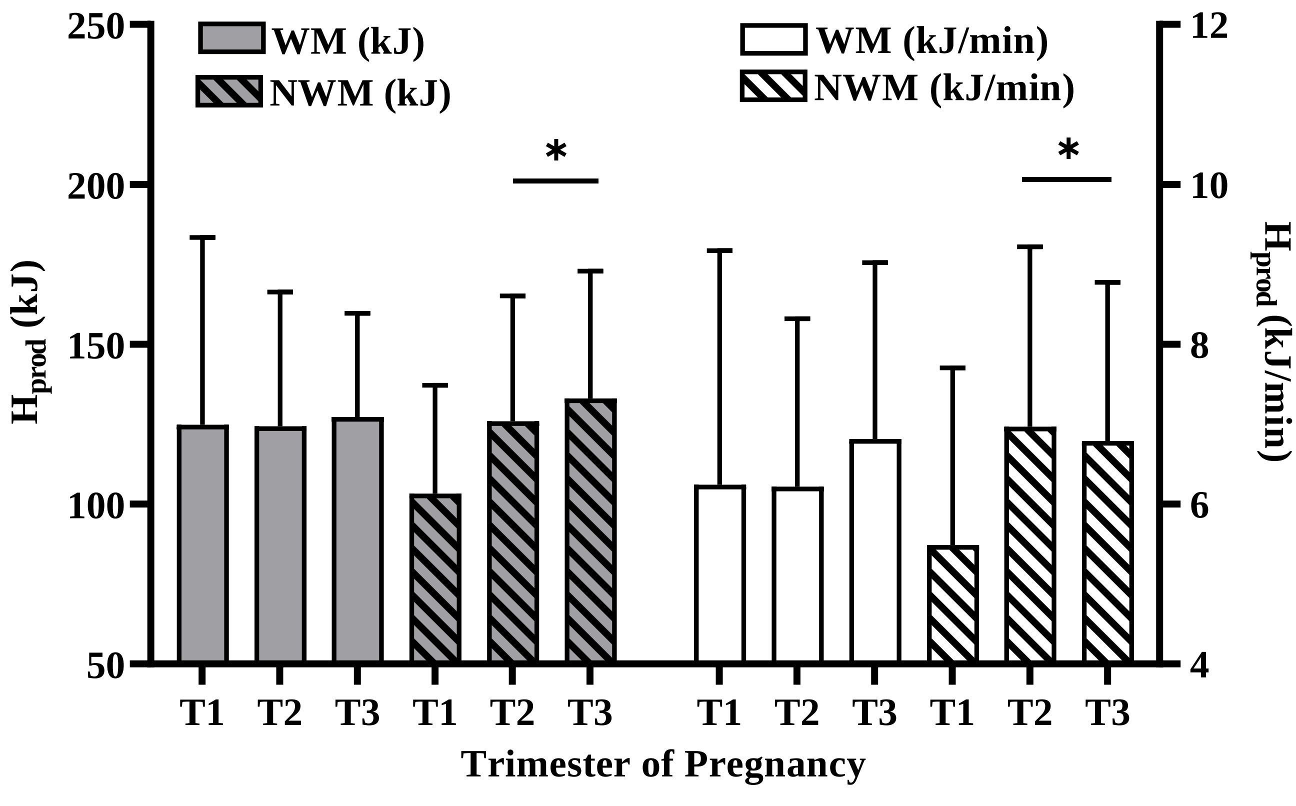

Figure 1. Resting energy expenditure (kJ and L/min) over the 20-minute rest period. Solid grey bars used for H_{prod} (kJ) and solid white bars for Hprod (kJ/min) in Weight-Matched (WM), T1 = early pregnancy, n = 14; T2 = mid-pregnancy 2, n = 14; T3 = late pregnancy, n = 14. Striped-grey bars represent H_{prod} (kJ) and striped, white bars for H_{prod} (kJ/min) in Non-Weight-Matched (NWM), T1, n = 23; T2, n = 53; T3, n = 33. *p < 0.05, significantly different from T1. Error bars represent SD.

3.2 Heart Rate Response during rest

Figure 2 displays the 1-minute average of heart rate (HR, bpm) at the end of 20-minutes of resting across pregnancy (T1, T2, and T3) in both WM and NWM groups. In the WM groups there was no main effect of pregnancy timepoint (P = 0.186), HR remained similar in T1 (73 ± 5 bpm) compared to both T2 (75 ± 9 bpm, P = 0.48) and T3 (77 ± 9 bpm, P = 0.15) with a group average of 75 ± 7 bpm. In the NWM group there was a main effect of pregnancy timepoint (P = 0.003), HR increased according to weight gain, compared to T1 (72 ± 7 bpm), HR was higher in T2 (75 ± 8 bpm, P = 0.03), and significantly greater in T3 (81 ± 9 bpm, P < 0.001).

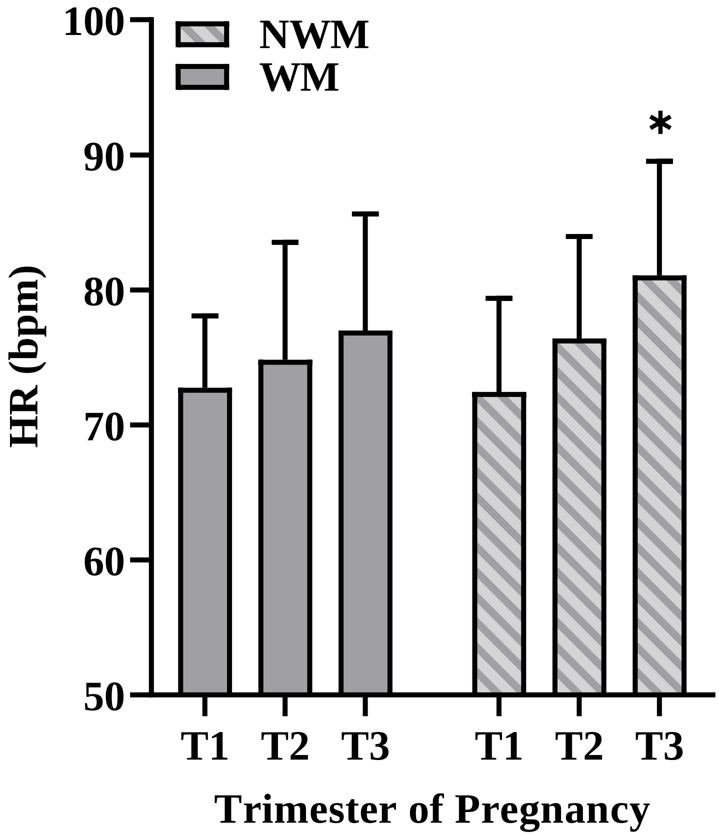

Figure 2. Average 1-minute Heart Rate (bpm) over the 20-minute of rest period. The solid grey bars represent the Weight-Matched (WM) group, T1 = early pregnancy, n = 14; T2 = mid-pregnancy 2, n = 14; T3 = late pregnancy, n = 14. The striped-grey bars represent the Non-Weight-Matched (NWM) group, T1, n = 23; T2, n = 53; T3, n = 33. *p < 0.05, significantly different from T1. Error bars represent SD.

Discussion

The purpose of this study was to investigate resting metabolic rate (RMR) from early, middle to late pregnancy, expressed as a rate (kJ/min) and sum (kJ) of heat production and heart rate (bpm). Overall, we found that women matched for total body weight (~71.6 kg) responded similarly across pregnancy (T1, T2, T3) in resting metabolic rate (i.e., expressed in kJ/min, kJ, and bpm). Furthermore, the women who were not matched for total body weight (difference of ~14.5 kg throughout pregnancy), demonstrated increased resting metabolic rate, measured in rate of heat production (kJ/min), sum of heat production (kJ), and heart rate (bpm) between pregnancy timepoints (T1, T2, T3).

In pregnancy, weight gain is comprised of the products of conception, including the fetus, placenta, and amniotic fluid, as well as maternal tissues containing breast, uterus, blood, fat stores and extra cellular fluid (Hytten & Leitch, 1971). Due to the cross-sectional inter-individual design of matching the total body weight of women in different pregnancy timepoints, the body composition from early to late pregnancy was vastly different. Women in early pregnancy timepoints are comparable to non-pregnant women of the same total body weight. However, for the same total body weight women in late pregnancy timepoints have approximately 3.8 kg of fetal related weight, that changes the composition of total body weight when compared to early pregnancy. Accordingly, a study by Lof *et al*.,2005 reported RMR in early pregnancy (i.e., between 8 – 20 weeks of gestation) to be similar to their pre-pregnant values (Lof *et al.*, 2005). Another that investigated resting metabolic rate employing the doubly-labeled water method in late pregnancy (i.e.,30 and 36 weeks gestation), reported a significantly higher resting metabolic rate than non-pregnant women (Forsum *et al.*, 1992). Our findings align with previous work, in that the pregnancy timepoints from T1, T2 to T3 along with an increase in body weight of ~ 14.5

kg, suggest a linear relationship with RMR (Forsum *et al.*, 1992; Goldberg *et al.*, 1993; Prentice *et al.*, 1996; Kopp-Hoolihan *et al.*, 1999; Butte *et al.*, 2004; Lof *et al.*, 2005; Melzer *et al.*, 2009).

The RMR varies according to differences in total body weight between pregnancy timepoints, an increase in total body weight comprises of both fat-mass and fat-free mass (Prentice *et al.*, 1989; Prentice *et al.*, 1995; Sparti *et al.*, 1997). In pregnancy, fat composition is predominantly within maternal tissue, the small fraction remaining is stored in fetus (Prentice *et al.*, 1989; Prentice *et al.*, 1995; Sparti *et al.*, 1997). Lederman *et al.*,1997 tested women between 14- and 37-weeks gestation, considered to be normal weight (i.e., BMI 19.8 – 26 kg/m2) and who gained within the recommended GWG range (i.e.,11.5-16 kg) and found them to have accrued approximately 4 kg of fat mass (Lederman *et al.*, 1997). In several studies, pregnant women considered to be underweight or overweight, that have gained outside the recommended GWG (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) resulted in considerable differences in fat-mass and fat-free mass compared to those who gained within GWG guidelines. The large differences in fat-mass and fat-free mass contribute to the variability in RMR independent of pregnancy (Dodd *et al.*, 2014; Petrella *et al.*, 2014; Poston *et al.*, 2015; Most *et al.*, 2018; Most *et al.*, 2019a). Maternal fat-mass is the most variable component of GWG, and gaining in excess of the recommended GWG guidelines (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) is highly prevalent worldwide (Chung *et al.*, 2013; Deputy *et al.*, 2015; Devlieger *et al.*, 2016). A longitudinal study by Butte *et al.,* 2003 reported that in those keeping within the GWG guidelines a linear increase in fat-mass of ~ 2kg per trimester can be accounted for over the course of pregnancy (Butte *et al.*, 2003). In the context of the findings by Butte *et al.*, 2003, the mean GWG in our non-weight matched group in T3 remained within the current IOM recommended guidelines

(I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009). However, five participants exceeded the recommended weight (i.e., GWG was about 19.5 kg) by approximately 3.5 kg (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009). In addition to the large differences in total body weight from T1 to T3 accounting for the increase in RMR, the reported increase in RMR in T3 compared to T1 may be accounted for by a large variability in fat-mass across pregnancy timepoints. Although, fat mass and fat-free mass were not measured in the current study, comparing RMR between pregnancy timepoints accounting for total body weight provided insight to the contribution of total body weight to RMR independent of pregnancy timepoint. The next step would be to account for the contribution of body composition in terms of the ratio of fat-mass and fat-free mass between pregnancy timepoints for a given total body weight.

Perspectives and Considerations

The outcomes from the present study provide valuable insight into the contribution of total body weight in RMR. However, given various measurement restrictions during pregnancy (inability to use dual x-ray absorptiometry or bio-impedance scale), measurements of fat-mass and fat-free mass were not accounted for within the groups and in the non-weight-matched group may have contributed to the variability in RMR across pregnancy (Dodd *et al.*, 2014; Petrella *et al.*, 2014; Poston *et al.*, 2015; Most *et al.*, 2018; Most *et al.*, 2019a). Considering exceeding GWG recommended guidelines (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) is very common among pregnant women, the contribution of fat-mass and fat-free mass no longer remains a linear increase when GWG is beyond the recommended guidelines. Future work should examine RMR in weight-matched pregnant women across T1, T2, and T3 that meet the recommended GWG guidelines (I.O.M & National Research

Council Committee to Reexamine Pregnancy Weight Guidelines, 2009), and compare to weight-matched women who significantly exceed the GWG guidelines, measuring both fat-mass and fat-free mass. A study in which pregnant women have the same total body weight, but vastly different fat-mass and fat-free mass ratios will offer further insight.

Conclusion

The present study was designed to compare RMR across pregnancy controlling for total body weight. By comparing groups of women of similar weight at each stage of pregnancy to those with increasing body weight with progressing pregnancy, we were able to demonstrate that if total body mass is the same RMR will respond accordingly. Therefore, the increase in total body weight influenced oxygen consumption (VO_2, L/min), heat production (kJ), and HR (bpm) as pregnancy progressed. In the future, it will be important to address the contribution of fat-mass and fat-free mass, considering their metabolic contributions to RMR.

References

Bronstein, M. N., Mak, R. P., & King, J. C. (1995). The thermic effect of food in normal-weight and overweight pregnant women. *Br J Nutr, 74*(2), 261-275. doi:10.1079/bjn19950129

Butte, N. F., Ellis, K. J., Wong, W. W., Hopkinson, J. M., & Smith, E. O. (2003). Composition of gestational weight gain impacts maternal fat retention and infant birth weight. *Am J Obstet Gynecol, 189*(5), 1423-1432. doi:10.1067/s0002-9378(03)00596-9

Butte, N. F., Wong, W. W., Treuth, M. S., Ellis, K. J., & O'Brian Smith, E. (2004). Energy requirements during pregnancy based on total energy expenditure and energy deposition. *Am J Clin Nutr, 79*(6), 1078-1087. doi:10.1093/ajcn/79.6.1078

Byrne, N. M., Groves, A. M., McIntyre, H. D., & Callaway, L. K. (2011). Changes in resting and walking energy expenditure and walking speed during pregnancy in obese women. *Am J Clin Nutr, 94*(3), 819-830. doi:10.3945/ajcn.110.009399

Carmichael, S., Abrams, B., & Selvin, S. (1997). The association of pattern of maternal weight gain with length of gestation and risk of spontaneous preterm delivery. *Paediatr Perinat Epidemiol, 11*(4), 392-406. doi:10.1046/j.1365-3016.1997.d01-28.x

Chung, J. G., Taylor, R. S., Thompson, J. M., Anderson, N. H., Dekker, G. A., Kenny, L. C., & McCowan, L. M. (2013). Gestational weight gain and adverse pregnancy outcomes in a nulliparous cohort. *Eur J Obstet Gynecol Reprod Biol, 167*(2), 149-153. doi:10.1016/j.ejogrb.2012.11.020

Clarke, P. E., Rousham, E. K., Gross, H., Halligan, A. W., & Bosio, P. (2005). Activity patterns and time allocation during pregnancy: A longitudinal study of british women. *Ann Hum Biol, 32*(3), 247-258. doi:10.1080/03014460500049915

Davies, G. A., Maxwell, C., McLeod, L., Gagnon, R., Basso, M., Bos, H., . . . Wilson, K. (2010). Sogc clinical practice guidelines: Obesity in pregnancy. No. 239, february 2010. *Int J Gynaecol Obstet, 110*(2), 167-173. doi:10.1016/j.ijgo.2010.03.008

Deputy, N. P., Sharma, A. J., & Kim, S. Y. (2015). Gestational weight gain - united states, 2012 and 2013. *MMWR Morb Mortal Wkly Rep, 64*(43), 1215-1220. doi:10.15585/mmwr.mm6443a3

Devlieger, R., Benhalima, K., Damm, P., Van Assche, A., Mathieu, C., Mahmood, T., Bogaerts, A. (2016). Maternal obesity in europe: Where do we stand and how to move forward?: A scientific paper commissioned by the european board and college of obstetrics and gynaecology (ebcog). *Eur J Obstet Gynecol Reprod Biol, 201*, 203-208. doi:10.1016/j.ejogrb.2016.04.005

Dodd, J. M., Turnbull, D., McPhee, A. J., Deussen, A. R., Grivell, R. M., Yelland, L. N., Robinson, J. S. (2014). Antenatal lifestyle advice for women who are overweight or obese: Limit randomised trial. *Bmj, 348*, g1285. doi:10.1136/bmj.g1285

Forsum, E., Kabir, N., Sadurskis, A., & Westerterp, K. (1992). Total energy expenditure of healthy swedish women during pregnancy and lactation. *Am J Clin Nutr, 56*(2), 334-342. doi:10.1093/ajcn/56.2.334

Gilmore, L. A., Butte, N. F., Ravussin, E., Han, H., Burton, J. H., & Redman, L. M. (2016). Energy intake and energy expenditure for determining excess weight gain in pregnant women. *Obstet Gynecol, 127*(5), 884-892. doi:10.1097/aog.0000000000001372

Goldberg, G. R., Prentice, A. M., Coward, W. A., Davies, H. L., Murgatroyd, P. R., Wensing, C., Sawyer, M. (1993). Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. *Am J Clin Nutr, 57*(4), 494-505. doi:10.1093/ajcn/57.4.494

Heini, A., Schutz, Y., Diaz, E., Prentice, A. M., Whitehead, R. G., & Jéquier, E. (1991). Free-living energy expenditure measured by two independent techniques in pregnant and nonpregnant gambian women. *Am J Physiol, 261*(1 Pt 1), E9-17. doi:10.1152/ajpendo.1991.261.1.E9

Hytten, F. E., & Leitch, I. (1971). *The physiology of human pregnancy*. London: Blackwell.

I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines IoM. (2009). The National Academies Collection: Reports funded by National Institutes of Health. *Weight Gain During Pregnancy: Reexamining the Guidelines*.

Kopp-Hoolihan, L. E., van Loan, M. D., Wong, W. W., & King, J. C. (1999). Longitudinal assessment of energy balance in well-nourished, pregnant women. *Am J Clin Nutr, 69*(4), 697-704. doi:10.1093/ajcn/69.4.697

Langford, A., Joshu, C., Chang, J. J., Myles, T., & Leet, T. (2011). Does gestational weight gain affect the risk of adverse maternal and infant outcomes in overweight women? *Maternal Child Health J, 15*(7), 860-865. doi:10.1007/s10995-008-0318-4

Lederman, S. A., Paxton, A., Heymsfield, S. B., Wang, J., Thornton, J., & Pierson, R. N., Jr. (1997). Body fat and water changes during pregnancy in women with different body weight and weight gain. *Obstet Gynecol, 90*(4 Pt 1), 483-488. doi:10.1016/s0029-7844(97)00355-4

Lof, M., & Forsum, E. (2006). Activity pattern and energy expenditure due to physical activity before and during pregnancy in healthy swedish women. *Br J Nutr, 95*(2), 296-302. doi:10.1079/bjn20051497

Lof, M., Olausson, H., Bostrom, K., Janerot-Sjöberg, B., Sohlstrom, A., & Forsum, E. (2005). Changes in basal metabolic rate during pregnancy in relation to changes in body weight and composition, cardiac output, insulin-like growth factor i, and thyroid hormones and in relation to fetal growth. *Am J Clin Nutr, 81*(3), 678-685. doi:10.1093/ajcn/81.3.678

Melzer, K., Schutz, Y., Boulvain, M., & Kayser, B. (2009). Pregnancy-related changes in activity energy expenditure and resting metabolic rate in switzerland. *Eur J Clin Nutr, 63*(10), 1185-1191. doi:10.1038/ejcn.2009.49

Melzer, K., Schutz, Y., Soehnchen, N., Othenin Girard, V., Martinez de Tejada, B., Pichard, C., Kayser, B. (2010). Prepregnancy body mass index and resting metabolic rate during pregnancy. *Ann Nutr Metab, 57*(3-4), 221-227. doi:10.1159/000322369

Most, J., Amant, M. S., Hsia, D. S., Altazan, A. D., Thomas, D. M., Gilmore, L. A., Redman, L. M. (2019). Evidence-based recommendations for energy intake in pregnant women with obesity. *The Journal of clinical investigation, 129*(11), 4682-4690. doi:10.1172/JCI130341

Most, J., Dervis, S., Haman, F., Adamo, K. B., & Redman, L. M. (2019). Energy intake requirements in pregnancy. *Nutrients, 11*(8), 1812. doi:10.3390/nu11081812

Most, J., Marlatt, K. L., Altazan, A. D., & Redman, L. M. (2018). Advances in assessing body composition during pregnancy. *Eur J Clin Nutr, 72*(5), 645-656. doi:10.1038/s41430-018-0152-8

Nielsen, B., & Davies, C. T. (1976). Temperature regulation during exercise in water and air. *Acta Physiol Scand, 98*(4), 500-508. doi:10.1111/j.1748-1716.1976.tb10342.x

Petrella, E., Malavolti, M., Bertarini, V., Pignatti, L., Neri, I., Battistini, N. C., & Facchinetti, F. (2014). Gestational weight gain in overweight and obese women enrolled in a healthy lifestyle and eating habits program. *J Matern Fetal Neonatal Med, 27*(13), 1348-1352. doi:10.3109/14767058.2013.858318

Piers, L. S., Diggavi, S. N., Thangam, S., van Raaij, J. M., Shetty, P. S., & Hautvast, J. G. (1995). Changes in energy expenditure, anthropometry, and energy intake during the course of pregnancy and lactation in well-nourished indian women. *Am J Clin Nutr, 61*(3), 501-513. doi:10.1093/ajcn/61.3.501

Poston, L., Bell, R., Croker, H., Flynn, A. C., Godfrey, K. M., Goff, L., . . . Briley, A. L. (2015). Effect of a behavioural intervention in obese pregnant women (the upbeat study): A multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol, 3*(10), 767-777. doi:10.1016/s2213-8587(15)00227-2

Prentice, A. M., Goldberg, G. R., Davies, H. L., Murgatroyd, P. R., & Scott, W. (1989). Energy-sparing adaptations in human pregnancy assessed by whole-body calorimetry. *Br J Nutr, 62*(1), 5-22. doi:10.1079/bjn19890004

Prentice, A. M., Poppitt, S. D., Goldberg, G. R., & Prentice, A. (1995). Adaptive strategies regulating energy balance in human pregnancy. *Hum Reprod Update, 1*(2), 149-161. doi:10.1093/humupd/1.2.149

Prentice, A. M., Spaaij, C. J., Goldberg, G. R., Poppitt, S. D., van Raaij, J. M., Totton, M., Black, A. E. (1996). Energy requirements of pregnant and lactating women. *Eur J Clin Nutr, 50 Suppl 1*, S82-110; discussion S110-111.

Rasmussen, K. M., Catalano, P. M., & Yaktine, A. L. (2009). New guidelines for weight gain during pregnancy: What obstetrician/gynecologists should know. *Curr Opin Obstet Gynecol, 21*(6), 521-526. doi:10.1097/GCO.0b013e328332d24e

Rousham, E. K., Clarke, P. E., & Gross, H. (2006). Significant changes in physical activity among pregnant women in the uk as assessed by accelerometry and self-reported activity. *Eur J Clin Nutr, 60*(3), 393-400. doi:10.1038/sj.ejcn.1602329

Spaaij, C. J., van Raaij, J. M., Van der Heijden, L. J., Schouten, F. J., Drijvers, J. J., De Groot, L. C., . . . Hautvast, J. G. (1994). No substantial reduction of the thermic effect of a meal during pregnancy in well-nourished dutch women. *Br J Nutr, 71*(3), 335-344. doi:10.1079/bjn19940142

Sparti, A., DeLany, J. P., de la Bretonne, J. A., Sander, G. E., & Bray, G. A. (1997). Relationship between resting metabolic rate and the composition of the fat-free mass. *Metabolism, 46*(10), 1225-1230. doi:https://doi.org/10.1016/S0026-0495(97)90222-5

CHAPTER 4

PREAMBLE TO ARTICLE 2

This chapter continues to investigate the influence of gestational weight gain on oxygen consumption, heat production, heart rate and rating of perceived exertion during incremental weight-bearing exercise testing from early, middle, to late pregnancy. The following study titled "Heat Production during Exercise in Pregnancy: Discerning the contribution of Phase of Pregnancy and Gestational Weight Gain." is presented in Chapter 4. This article will be submitted to European Journal of Sports Science.

Title:

Heat Production during Exercise in Pregnancy: Discerning the contribution of Total Body Weight.

Authors:

Sheila Dervis[1], Danilo F da Silva[1], Carla Geurts[1], François Haman[1], Kristi Bree Adamo[1]*

Author Affiliations:

[1] Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, Ottawa, ON, Canada, K1N 6N5.

Corresponding Author:

Dr. Kristi B. Adamo

Associate Professor

School of Human Kinetics, Faculty of Health Sciences

Lees Campus, E 250F

200 Lees Ave. Ottawa, ON K1N 6N5

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Abstract

Background: While many studies report enhanced thermoregulatory function as pregnancy progresses, it is unclear if differences are attributed to weight gain or other physiological changes throughout pregnancy. The purpose was to compare the sum and rate of heat production (H_{prod}), heart rate (HR) and rating of perceived exertion (RPE) during weight-bearing exercise between weight-matched (WM) and non-weight matched (NWM) groups across pregnancy timepoints.

Methods: A cross-sectional design of healthy pregnant women at different pregnancy timepoints (early, T1; middle, T2; late, T3), performed a 7-stage weight-bearing incremental exercise protocol. Measurements of H_{prod} (kJ & kJ/min), HR (bpm) and RPE (Borg scale, 6 to 20) were taken. Two experimental groups were studied: 1) WM - matched for total body weight, 2) NWM – not matched for total body weight; in T1, T2, and T3.

Results: During exercise, equivalent H_{prod} at T1 (326 ± 88 kJ), T2 (330 ± 43 kJ), and T3 (352 ± 52 kJ) ($P = 0.504$), HR ($P = 0.830$), and RPE ($P = 0.195$) between T1, T2, and T3 were observed in the WM group. In the NWM group, H_{prod} (kJ, from stages 1 to 6 of the exercise) increased as pregnancy timepoints progressed from T1 (291 ± 76 kJ) to T2 (347 ± 41 kJ, $P < 0.001$) and T3 (385 ± 47 kJ, $P < 0.001$). HR increased from T1 to T3 in warm-up to stage 6 of exercise ($P = 0.009$). RPE did not change as pregnancy timepoint progressed in the NWM group ($P = 0.309$).

Conclusion: Total body weight irrespective of pregnancy timepoint significantly modulates physiological measurements of H_{prod} and HR during exercise. Therefore, to compare thermoregulatory function between pregnancy-time points during exercise, it is crucial to account for total body weight.

Keywords: Thermoregulation, pregnancy, heat production, oxygen consumption, exercise intensity, weight.

1.0 Introduction

Exercise is highly beneficial throughout pregnancy for both maternal and fetal health (Mottola *et al.*, 2018b). Advantages gleaned from exercising during pregnancy include better management of gestational weight gain (GWG) and a lower risk of adverse health outcomes (Nascimento *et al.*, 2012; Davenport *et al.*, 2018b). Furthermore, the Society of Obstetricians and Gynaecologists of Canada (SOGC), the Canadian Society for Exercise Physiology (CSEP) and the American College of Obstetricians and Gynecologists (ACOG) have developed physical activity guidelines for pregnant women (Mottola *et al.*, 2018b; 2020). The SOGC/CSEP and ACOG recommend that, in the absence of any medical or obstetrical contraindications, pregnant women engage in at least 150 minutes per week of moderate-intensity aerobic and strength conditioning exercise, during most or all days of the week (Mottola *et al.*, 2018b; 2020) . Systematic reviews report that compared to sedentary pregnant women, physically active women, report less musculoskeletal pain, depressive symptoms, GWG, and postpartum weight retention, urinary incontinence as well as gestational diabetes and insulin resistance (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009; Medek *et al.*, 2016). Despite the apparent maternal and fetal health benefits of exercise, only a small portion of pregnant women meet the recommended physical activity guidelines. One concern pregnant women have previously reported when considering engaging in exercise programs is the potential teratogenic risk of overheating (Clarke & Gross, 2004; Franklin *et al.*, 2017b).

A maternal core temperature exceeding 39.0°C or an approximately 1.5 to 2.0°C increase from resting has been considered the critical threshold for an increased risk for teratogenic outcomes to a fetus (Graham *et al.*, 1998; Miller *et al.*, 2002). Changes in cardiovascular function, including increases in blood volume, stroke volume, cardiac output, heart rate (HR), and decrease in systemic vascular resistance (Metcalfe & Ueland, 1974; Tan & Tan, 2013), occur during pregnancy and are key modulators of the body's capacity to dissipate heat (Hartmann & Bung, 1999; Soultanakis-Aligianni, 2003). Plasma and blood volume gradually increase by 40-50% throughout pregnancy to accommodate a growing and developing fetus, increasing HR (15 beats/min more than usual), stroke volume, and cardiac output (Spatling *et al.*, 1992; Hartmann & Bung, 1999). Systemic vascular resistance also drops due to smooth muscle relaxation and overall vasodilation caused by elevated progesterone, leading to a fall in blood pressure (Hartmann & Bung, 1999). Increases in blood flow appear to counteract the elevation of heat storage via dry heat loss (Metcalfe & Ueland, 1974; Spatling *et al.*, 1992). Simply put, a greater amount of comparatively cooler blood is transported from the periphery to the core, lowering overall body temperature. Fetal temperature depends upon maternal temperature, the metabolic rate of the fetus, and uterine blood flow, with the major effect exerted by the maternal temperature (Clapp, 1991; Hartgill *et al.*, 2011). Fetal growth and development results in a considerable amount of heat production (Hartgill *et al.*, 2011) and to maintain thermal balance, the heat produced from the fetus is transferred to the mother before being dissipated to the environment via placenta exchange through the umbilical cord (Hartgill *et al.*, 2011). Any deficiencies in heat exchange from fetus, via mother, to the environment could result in elevations in maternal core temperature increasing risks of teratogenesis (Miller *et al.*, 2002)

The predominant consensus regarding the modifications in thermoregulatory capacity that occur during pregnancy consists of an overall enhancement in dry (i.e., improved cardiovascular function) (Vähä-Eskeli *et al.*, 1991a; Szymanski & Kogutt, 2018), and evaporative heat loss (i.e., whole body sweat loss) (Jones *et al.*, 1985; Clapp, 1991). Furthermore, across pregnancy, core temperature responses at rest and during exercise are lower in late- compared to early- pregnancy and non-pregnant women (Jones *et al.*, 1985; Clapp *et al.*, 1987; Soultanakis, 2016). However, the findings of a lower core temperature response during exercise in late- compared to early-pregnancy may be confounded by a commonly used methodology that does not account for large differences in total body weight between pregnancy timepoints. For example, during a fixed intensity (~61-64% VO_{2peak}) treadmill exercise, thermoregulatory responses, including core temperature and sweating, were compared from 8 weeks gestation with a total body weight of about 62 kg to 36 weeks gestation at about 79 kg (Clapp, 1991). The dramatic difference in body weight was not considered and poses a problem in interpretation knowing that the rise in core temperature, directed by the rate of change in heat production (H_{prod}), is a result of the intensity and duration of weight-bearing exercise and total body weight. Throughout pregnancy, many physiological changes occur, including weight gain to accommodate a growing fetus, and authors observed a 17 kg difference from early to late pregnancy (Clapp, 1991). Looking at total body weight alone, a greater weight provides a bigger heat sink (Havenith *et al.*, 1998); therefore, exercise at a fixed rate of exercise intensity should theoretically lead to a smaller rise in core temperature due to the progressively greater weight from early to late pregnancy. As would be expected, the authors reported an attenuation in the rise of core temperature from early compared to late gestation (Clapp, 1991).

Although previous studies markedly improved our understanding of the thermoregulatory responses to exercise during pregnancy, we possess limited information on the influence of total body weight on H_{prod} during weight-bearing exercise. The inconclusive information on integrated influences of total body weight on H_{prod} during exercise from early to late pregnancy represents an important gap in our understanding of thermoregulatory responses. Given the importance of distinguishing between total body weight and pregnancy as factors influencing H_{prod}, the primary purpose of this study was to compare both the sum and rate of heat production (i.e., H_{prod} in kJ and kJ/min), hear rate (HR), and rating of perceived exertion (RPE) responses during a weight-bearing exercise. This study used an inter-individual cross-sectional design. Women between early, T1; middle, T2; and late, T3 pregnancy timepoints were either matched or not matched for total body weight and performed an exercise protocol.

2.0 Methods

2.1 Ethical Approval

This study examined women participating in the CIHR-funded trial, PhysicaL Activity and dietary implicatioNs Throughout pregnancy (PLACENTA) study (MOP-142298). The PLACENTA protocol was approved by numerous research ethics boards across Ottawa: University of Ottawa (#H11-15-29), Ottawa Health Sciences Network (REB# 20160178-01H), Children's Hospital of Eastern Ontario (REB# 16/68X), Queensway Carleton Hospital (File# 17-03), and Hôpital Montfort (#LG-01-06-16). The study was performed following the Declaration of Helsinki. All participants provided written, informed consent before participation.

2.2 Study Participants

All pregnant participants were selected from those who identified interest in participating in the PLACENTA study. Participants were recruited from regional hospitals, midwifery centres, university campuses, and social media platforms. The inclusion criteria for the pregnant participants consisted of the following: 18 to 40 years old, ability to communicate in either English or French, carrying a singleton fetus, self-reporting a body mass index (BMI) (pre-pregnancy) of normal or overweight (18.5-29.9 kg/m^2), having stable weight (± 5 kg) for a minimum of 6 months before pregnancy, and having no contraindications to exercise. Exclusion criteria were as follows: habitual consumption of alcohol/drugs/tobacco, pre-pregnancy diabetes, untreated thyroid disease, or hypertension. The first visit was in the early stage of pregnancy; between weeks 12 and 18 (T1). The second visit took place during the middle stage of pregnancy: between weeks 24 and 28 (T2), and a third visit occurred late in pregnancy; between weeks 34 and 38 of gestation (T3). The participants were asked to refrain from exercise 24 hours before the visit.

2.3 Anthropometric Measures

All participants wore exercise clothes, and a trained research team member measured their height and body mass for each visit (T1, T2 and T3). Height (cm) was measured using a stadiometer (HR-200 Wall-Mounted Height Rod, Tanita Corporation of America Inc., Illinois, USA) in duplicate and reported to the closest 0.1 cm. The participants were barefoot, and the measurement was taken at the end of a normal exhalation. Body mass (kg) was measured using an electronic scale (BWB-800 Doctors Scale, Tania Corporation of America Inc., Illinois, USA), and was recorded to the nearest 0.1 kg. The participants were barefoot, only wearing their exercise clothes, and body mass was measured at the beginning of all study visits. GWG was calculated as the difference in measured T1, T2, and T3 body mass and self-reported pre-pregnancy weight. This difference was reported in kilograms (kg). The percentage of upper limit of GWG guidelines for a woman's specific gestational age (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) was used to define the %GWG within each pregnancy timepoint that remained within the within normal (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) guidelines For example, if a woman had started pregnancy with a BMI categorized as normal, and gained 8.1 kg by 27 weeks' gestation, given the upper limit of weight gain for that week of pregnancy is 9 kg, she would be at 90% of GWG guideline (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009).

2.4 Physical activity levels

At each of the three pregnancy timepoints, participants were provided with an omniaxial Actical® accelerometer (Philips Respironics, QC, Canada) and received instructions to wear the device for the following seven days on their hip during waking hours only (i.e., not for sleeping or bathing). A minimum of three valid days is required to include the Actical® data from pregnant women in the analysis (da Silva *et al.*, 2020). A valid day is considered a day with at least 10 hours of wear. Data were analyzed using SAS version 9.4 (SAS Institute, NC, USA) following the Canadian Health Measures Survey analytical guidelines (Colley *et al.*, 2010). Cut-offs for accelerometer count range representing moderate-to-vigorous physical activity were ≥ 1,535 (Colley *et al.*, 2010). Moderate-to-vigorous physical activity was expressed as min/day.

2.5 Metabolic Measurements

Before the start of the baseline period (i.e., 20 min of resting measurements), the mass flow generator (FK500, Sable Systems International Inc, Las Vegas, NV USA) was set at 100 L/min, at standard temperature, pressure and dry (STPD) conditions. Following the rest period and before starting exercise, the mass flow generator (FK500, Sable Systems International Inc, Las Vegas, NV USA) was increased to 250 L/min, at STPD conditions. Throughout testing, barometric pressure (P_B) and the composition of inspired (f_i) and expired (f_e) air were measured from a 250 mL/min subsample using a field metabolic system (Sable Systems International Inc., Las Vegas, USA).

Measurements were taken continuously (i.e., breath by breath) throughout both baseline and exercise protocols. VO_2 (in L/min) was calculated from fiO_2 and $fiCO_2$ (inspired fractions of the measured gas in ambient air); and feO_2 and $feCO_2$ (expired fractions of the measured gas exiting the mouthpiece). All measured gases measured were corrected for the partial pressure of water (P_{H2O}).

Heat Production (H_{prod})

Metabolic Energy Expenditure ($\dot{M}$) (i.e., metabolic rate) in kJ and kJ per min, was calculated using the respiratory exchange ratio (RER = VCO_2/ VO_2) and the caloric energy equivalents for carbohydrates (e_c, 21.13 kJ per L of O_2 consumed) and fat (e_f, 19.62 kJ per L of O_2 consumed) in the following equation (Nielsen & Davies, 1976):

$$\dot{M}\ (kJ/min) = \left[\dot{v}O_2\ \left(\frac{L}{min}\right) \times \left(\frac{RER-0.7}{0.3} \cdot e_c + \frac{1-RER}{0.3} \cdot e_f\right)\right]$$

In which VO_2 (L/min) and VCO_2 (L/min) values are reported in STPD conditions.

External work output in kJ per min, was calculated throughout the treadmill walking protocol. The calculation used the participant's body mass (kg), set speed (m/min), and vertical distance travelled in meters (i.e., % incline) on a calibrated treadmill as the parameters in the following equation:

$$External\,Work\ (kJ/\mathrm{min}) = \ body\,mass\ (kg) \times \ speed\ \left(\frac{m}{min}\right) \times \left(Sin(\Theta) \cdot 0.0098 \left(\frac{kJ}{kg \cdot m}\right)\right)$$

H_{prod} in kJ was calculated as the difference between (M) and external work output (H_{prod} = M – External Work).

2.6 Data Collection & Experimental Protocol

All laboratory visits occurred in the morning between 6h00 and 10h00, and after an 8-hour fast. Following anthropometric measurements, the participants were given a standardized snack consisting of juice (orange or cranberry flavour), a granola bar, and fruit (~ 370 kcals). After the standardized snacks were consumed, participants were instrumented with a HR chest strap (Polar V800, Polar Electro Canada) and fitted with a metabolic mask, where expired gases were drawn into a T-type, one-way, non-rebreathing valve (Series 2700 Large: Hans-Rudolph, Shawnee, KS).

Once instrumented, participants completed an incremental exercise protocol. The incremental exercise protocol is a variation of the modified HALO submaximal treadmill protocol (Breithaupt *et al.*, 2012). In brief, the test consists of a 4 min warm-up at a walking speed of 3.2 km/h and 0% incline, followed by seven 3-min walking stages continuing at a pace of 3.2 km/h with the incline increasing 2% to a maximum of 14% by stage seven. Throughout the exercise test, continual measurements of the participants' respiration, HR and RPE (Borg's 15-point scale) (Borg, 1982) were collected. If the participants did not stop the test volitionally, the cut-off to end exercise was 85% of the maximum HR (calculated by 0.85 × 220-age), considered to achieve a moderate intensity of exercise. After completing the incremental exercise protocol, participants cooled down for 2 min at a speed of 1.6 km/h and 0% grade.

2.7 Experimental groups

We examined women in early (T1), middle (T2) and late (T3) pregnancy timepoints independently and separated participants into two experimental groups based on total body mass (kg) as a cross-sectional inter-individual design (i.e., there are six different groups). In the weight-matched group (WM), participants in T1, T2 and T3 of pregnancy were matched for total body weight. In this case, we selected women who had a body weight ~ 70k regardless of timepoint. In the non-weight-matched group (NWM), participants in T1, T2 and T3 of pregnancy had varying total body weight. As shown in Table 1, other important parameters were comparable for participants in both groups including height, age, gestational weight gain, baby weight, and placental weight. The pre-pregnancy BMI (kg/m^2) reported by all participants were within normal weight (18.5 – 24.9 kg/m^2) and overweight (25 – 29.9 kg/m^2) categories. Participants who visited the lab in T1, T2, and T3 pregnancy timepoints were not initially matched for weight during the experimental session. Participants were retrospectively categorized into WM and NWM groups, as such, the sample sizes for each time point were different.

2.8 Statistical Analysis

All statistical analyses were completed using SPSS statistical software (Version 27.0 for Windows; IBM, Armonk, NY) and were conducted separately for the WM and the NWM groups. Descriptive statistics were performed for participant characteristics include maternal age, height, weight, gestational weight gain, weeks of gestation, baby weight, and placenta weight. All values were reported as means ± standard deviation (SD) unless otherwise stated. The frequency of women classified with normal weight BMI in each pregnancy timepoint was compared using the Chi-square test or Likelihood ratio. One-way analysis of variance (ANOVA) was used to compared T1, T2, and T3 in both experimental groups. When significant differences were observed, *post hoc* analysis was performed using Bonferroni correction. For all analyses, the significance was set at $p \leq 0.05$.

H_{prod} (kJ/min), H_{prod} (kJ), HR (bpm) and RPE during exercise were analyzed separately between the two experimental groups: 1) weight-matched (WM) and 2) non-weight-matched (NWM). Comparisons of responses to exercise (i.e., incremental exercise protocol) across T1, T2, and T3 were analyzed using a two-way mixed ANOVA for repeated measures. Where appropriate, all p-values were adjusted for multiple comparisons using the Bonferroni correction. H_{prod} (kJ/min), HR, and RPE values were plotted as a function of stage of exercise, and comparisons at baseline and across all exercise stages were made from warm-up to the last stage of exercise. H_{prod} (kJ/min) and HR were computed as the average of the last 1-minute for each exercise stage. RPE values collected in the last 30 seconds of each stage were computed for analysis. H_{prod} was plotted as a function of the baseline period (20 min) and stages of exercise (22 min).

3.0 Results

Participant characteristics for both WM and NWM groups are described in Table 1. As designed, women across T1, T2, and T3 in both WM and NWM groups were similar in age and height. Moderate-to-vigorous physical activity was not significantly different between T1, T2, and T3 for both WM and NWM groups. In the WM group, fourteen pregnant women in each T1, T2 and T3 were matched for body mass (kg). In the NWM group, we were able to test twenty-three participants in T1, fifty-three participants in T2, and thirty-three participants in the T3. All WM and NWM groups were able to complete the first six stages (not including the warm-up) of exercise successfully, following our protocols to stop exercise. Eleven participants did not complete the last stage of the incremental exercise protocol (i.e., 3.2 km/h; 14% incline). We opted to include only data up to stage 6 of the incremental exercise protocol to avoid missing data for the analysis.

Table 1. Participant characteristics for weight-matched and non-weight matched pregnant women

	Trimester of Pregnancy					
	Weight-Matched (WM)			Non-Weight-Matched (NWM)		
	T1	T2	T3	T1	T2	T3
Age (years)	32 ± 4	32 ± 3	33 ± 4	32 ± 3	32 ± 3	32 ± 3
Gestational age (weeks)	15.2 ± 0.7	26.8 ± 1.2	35.8 ± 1.6	15.8 ± 0.9	27.2 ± 1.6	36.1 ± 1.8
Height (metres)	1.68 ± 0.07	1.66 ± 0.05	1.64 ± 0.05	1.67 ± 0.08	1.68 ± 0.06	1.67 ± 0.06
Body mass (kg)	71.6 ± 8.1	71.7 ± 8.0	71.5 ± 7.6	65.4 ± 8.9	74.8 ± 9.7*	79.9 ± 8.9*
Pre-pregnancy BMI (kg/m^2)	24.8 ± 2.5	22.9 ± 3.0	21.5 ± 1.8	22.4 ± 2.2	23.3 ± 2.8	23.1 ± 2.3
Pre-pregnancy BMI (% within ‘normal weight’ category)	57.1	78.6	100[†]	91.3	77.4	81.8
Baby weight (kg)	3.319 ± 0.353	3.068 ± 0.248	3.282 ± 0.386	3.302 ± 0.373	3.302 ± 0.373	3.293 ± 0.362
Placenta weight (kg)	0.588 ± 0.076	0.514 ± 0.082	0.559 ± 0.077	0.575 ± 0.097	0.575 ± 0.097	0.585 ± 0.101
GWG (kg)	2.0 ± 1.3	7.8 ± 3.3*	12.7 ± 3.8*,#	2.8 ± 1.8	8.9 ± 3.0*	13.2 ± 4.0*#
GWG (% upper limit IOM)	72.3 ± 47.6	95.2 ± 37.2	96.3 ± 27.7	90.8 ± 67.4	110.0 ± 37.3	103.0 ± 27.9
MVPA (min/day)	32.4 ± 19.6	23.2 ± 25.9	14.7 ± 18.0	32.7 ± 24.4	24.3 ± 19.7	19.0 ± 13.9

BMI = body mass index; GWG = gestational weight gain; MVPA = moderate-to-vigorous physical activity. Values are presented as mean ± SD. Weight-Matched (WM), T1 = early pregnancy, n = 14; T2 = mid-pregnancy 2, n = 14; T3 = late pregnancy, n = 14. Non-Weight Matched (NWM), T1, n = 23; T2, n = 53; T3, n = 33. For MVPA (WM), T1 n = 12; T2 n = 12; T3 n = 11. For MVPA (NWM), T1 n = 21; T2 n = 41; T3 n = 23. *$p < 0.05$, significantly different from T1. #$p < 0.05$, significantly different from T2. †$p < 0.05$, Likelihood ratio for WM. Gestational weight gain, baby and placenta weight taken from participants in the T3 group of weight-matched (n = 13) and non-weight matched group (n = 24).

3.1 H_{prod}, HR and RPE during baseline and exercise in WM group.

The sum of H_{prod} during baseline was not significantly different ($p = 0.984$) from T1 (125 ± 59 kJ), T2 (124 ± 42 kJ), to T3 (127 ± 32 kJ). In Figure 1, the sum of H_{prod} (kJ) throughout the entire incremental exercise protocol from warm-up to the end of stage 6 of exercise in the WM group, was similar ($p = 0.504$) at T1 (326 ± 88 kJ), T2 (330 ± 43 kJ), and T3 (352 ± 52 kJ).

In Figure 2A, rate of H_{prod} (kJ/min) taken as a 1-minute average at the end of each stage of the exercise protocol from baseline to stage 6 of exercise, an effect of exercise stage was found in the WM group as H_{prod} (kJ/min) increased from baseline to stage 6 (all, $p < 0.001$) across pregnancy. There was no main effect of pregnancy timepoint on the H_{prod} (kJ/min) response ($p = 0.273$). Furthermore, there was no interaction between exercise and pregnancy, meaning the increase of H_{prod} (kJ/min) was similar from baseline to stage 6 of exercise in T1, T2, and T3 ($p = 0.649$).

Figure 3A illustrates the HR response across pregnancy in baseline and during exercise. The WM group showed an effect of exercise stage as HR significantly increased from baseline to stage 6 (all, $p < 0.001$). No main effect of pregnancy timepoint on HR was observed ($p = 0.549$). Correspondingly, there was no interaction between exercise stage and pregnancy timepoint for HR ($p = 0.830$).

Figure 4A shows the RPE scale responses. The WM group demonstrated an effect of exercise stage as RPE significantly increased from warm-up to stage 6 (all, $p < 0.001$). There was no main effect of pregnancy timepoint on RPE from warm-up to stage 6 of exercise ($p = 0.195$). Moreover, there was no interaction between exercise stage and pregnancy timepoint, in that the increase in RPE was similar from warm-up to stage 6 of exercise between T1, T2, and T3 ($p = 0.089$).

3.2 H_{prod}, HR and RPE during baseline and exercise in NWM group

The sum of baseline H_{prod} (kJ) at T1 (103 ± 34 kJ) was significantly lower than T2 (126 ± 39 kJ, $p = 0.047$) and T3 (133 ± 40 kJ, $p = 0.012$). However, H_{prod} (kJ) did not significantly change between T2 and T3 in the baseline ($p = 0.671$). In Figure 1, H_{prod} (kJ) throughout the entire incremental exercise protocol from warm-up to the end of stage 6 of exercise in the NWM group was significantly different between T1, T2 and T3 ($p < 0.001$). The *post hoc* comparisons revealed a progressive increase in H_{prod} from T1 (291 ± 76 kJ) to T2 (347 ± 41 kJ, $p < 0.001$) and T3 (385 ± 47 kJ, $p < 0.001$). Also, there was a significant increase in H_{prod} from T2 to T3 ($p = 0.003$). In Figure 2B, the rate of H_{prod} (kJ/min), taken as a 1-minute average at the end of each stage of the exercise protocol from baseline to stage 6 of exercise, was presented for the NWM group. There was an effect of exercise stage as H_{prod} (kJ/min) increased from baseline to stage 6 (all, $p < 0.003$). In addition, an interaction was uncovered between the stage of exercise and pregnancy timepoint as H_{prod} (kJ/min) significantly increased from T1, T2 to T3 during exercise ($p < 0.003$).

In Figure 3B, the HR increased from T1, T2, to T3 ($p < 0.001$) in the NWM group. An effect of exercise stage was identified as HR increased from baseline to stage 6 of exercise (all, $p < 0.001$). We also found an interaction between exercise stage and pregnancy timepoint for HR ($p = 0.009$). The increase in HR was significantly greater in T3 than T1 and T2 ($p = 0.009$), although it was similar in T1 compared to T2 ($p = 0.552$).

Figure 4B presents the RPE scale responses in the NWM group. From warm-up to stage 6 of exercise across all pregnancy timepoints there was an effect of exercise stage on RPE (all, $P<0.001$). There was no main effect of pregnancy timepoint on RPE ($P = 0.309$). Accordingly, there was no interaction between exercise stage and pregnancy timepoint ($P = 0.479$).

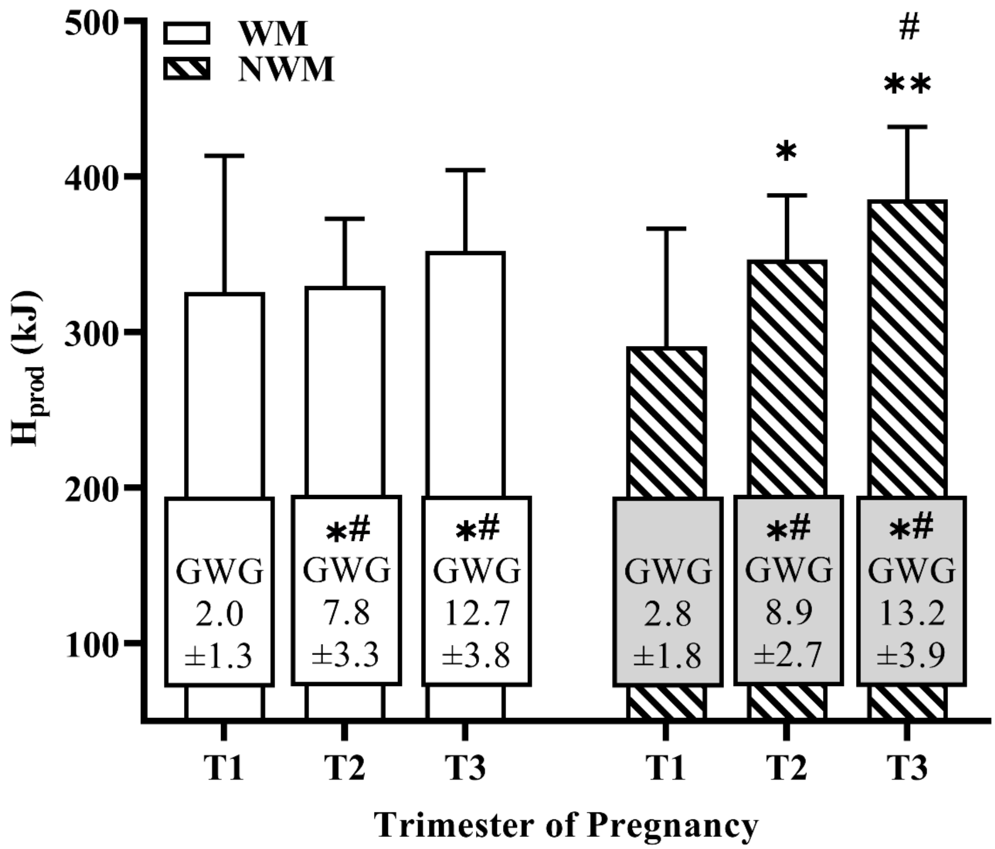


Figure 1. Sum of heat production H_{prod} (kJ) over a 22-minute incremental exercise protocol. White bars are Weight-Matched (WM), T1 = early pregnancy, n = 14; T2 = mid-pregnancy 2, n = 14; T3 = late pregnancy, n = 14. Stripped bars are Non-Weight-Matched (NWM), T1, n = 23; T2, n = 53; T3, n = 33. T1 significantly different from T2 *p < 0.001; and T3 **p < 0.001 for the same group. T2 significantly different from T3 #p < 0.003 for the same group. Error bars represent SD. For both WM and NWM groups the GWG in T1 is significantly different from T2 and T3, †p <
0.001.

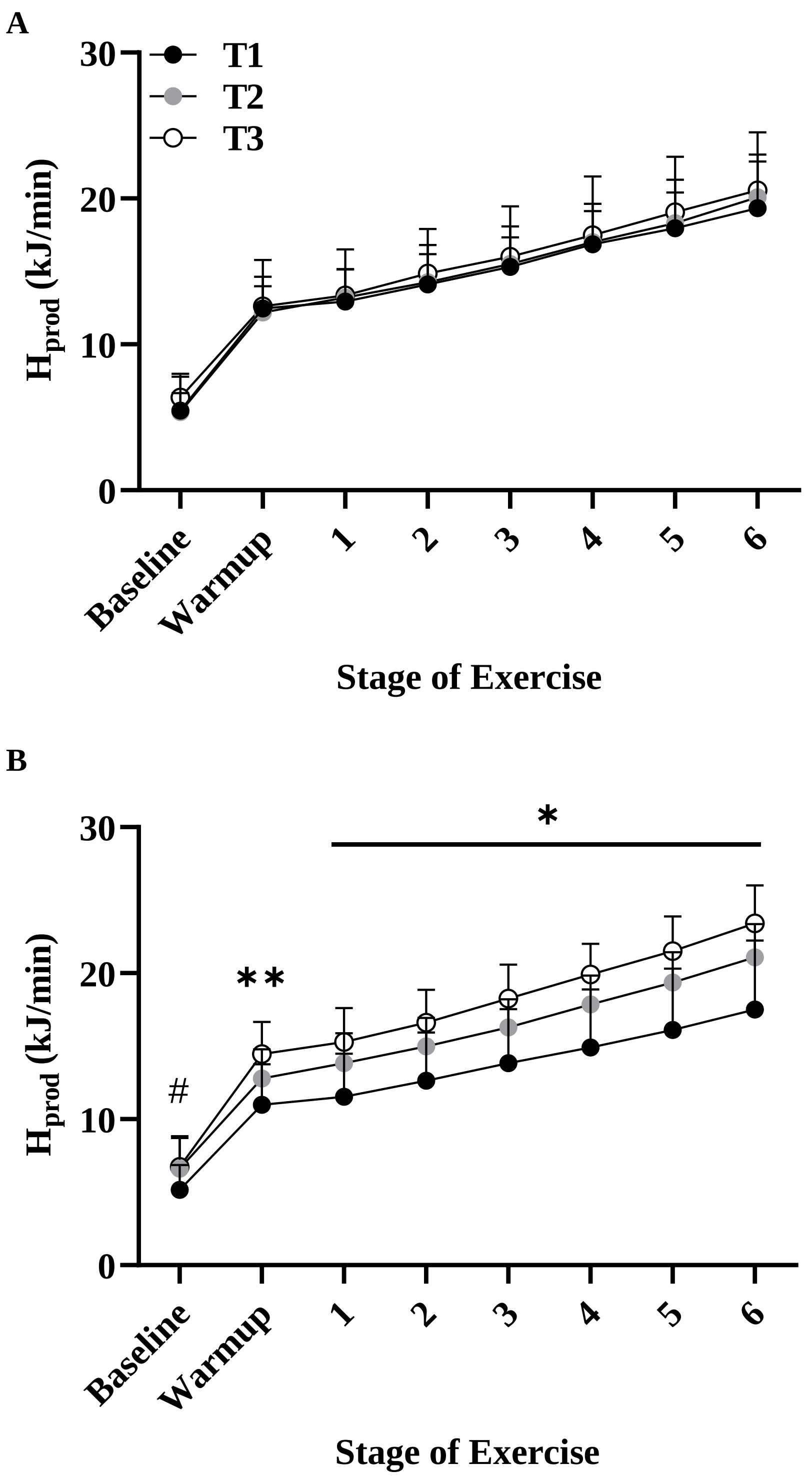


Figure 2. Rate of heat production H_{prod} (kJ/min), minute average from baseline to stage 6 of the incremental exercise protocol. A) Weight-Matched (WM), T1 (black circles) = early pregnancy, n = 14; T2 (grey circles) = mid-pregnancy 2, n = 14; T3 (white circles) = late pregnancy, n = 14. B) Non-Weight-Matched (NWM), T1, n = 23; T2, n = 53; T3, n = 33. In baseline, T1 significantly lower than T2 and T3 # $p < 0.041$; In warm-up, T1 significantly lower than T3 ** $p < 0.008$; Exercise stages 1 to 6, T1 significantly lower than both T2 and T3; T2 significantly lower than T3, *$p < 0.005$. Error bars represent SD.

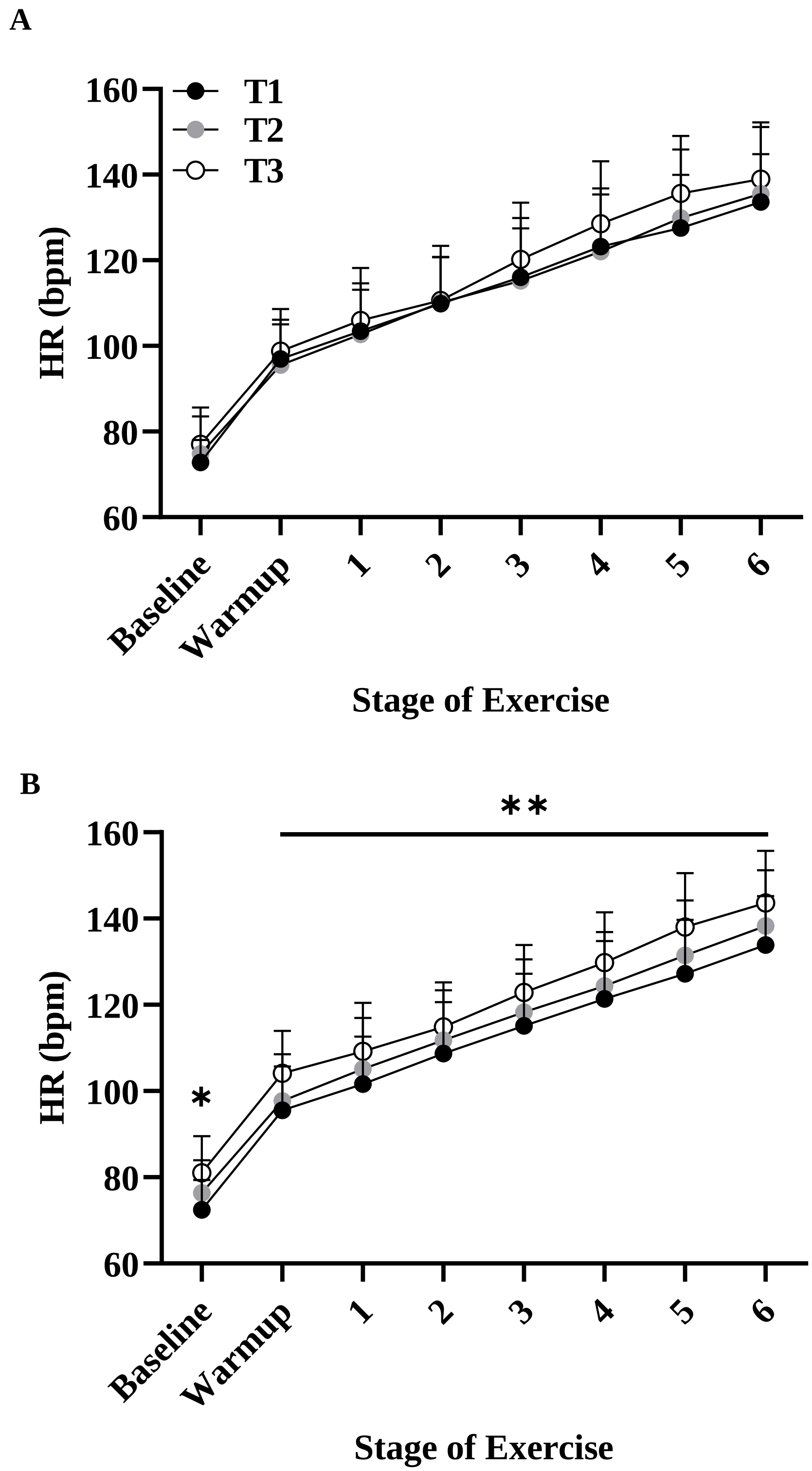
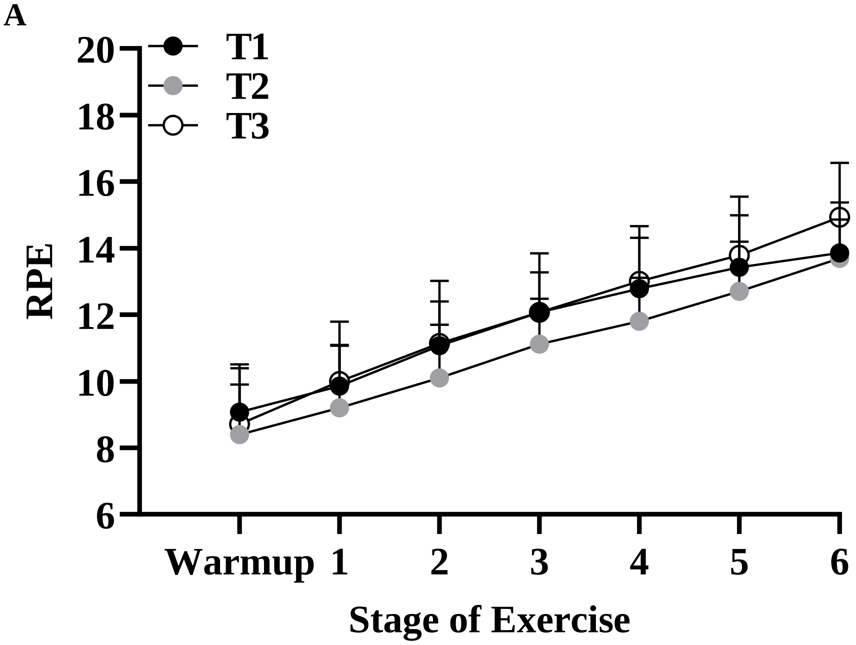


Figure 3. Heart Rate (bpm), minute average from baseline to stage 6 of the incremental exercise protocol. A) Weight-Matched (WM), T1 (black circles) = early pregnancy, n = 14; T2 (grey circles) = mid-pregnancy 2, n = 14; T3 (white circles) = late pregnancy, n = 14. B) Non-Weight-Matched (NWM), T1, n = 23; T2, n = 52; T3, n = 32. In baseline, T1 significantly lower than T2 and T3; T2 significantly lower than T3 *p < 0.009; In warm-up and exercise stages 1 to 6, T1 significantly lower than T3 **p < 0.009. Error bars represent SD.

A



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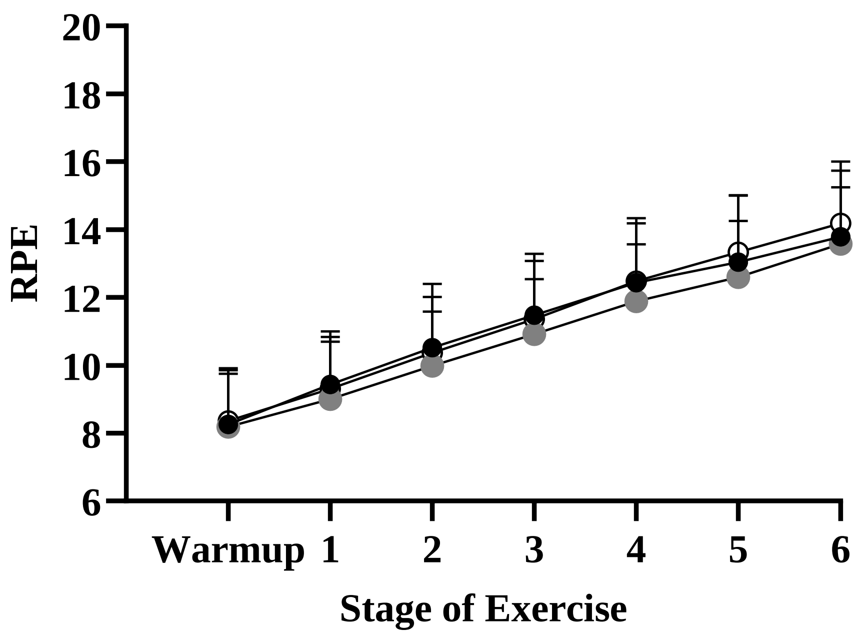

Figure 4. Rate of perceived exertion (RPE) from warm-up to stage 6 of the incremental exercise protocol. A) Weight-Matched (WM), T1 (black circles) = early pregnancy, n = 14; T2 (grey circles) = mid-pregnancy, n = 14; T3 (white circles) = late pregnancy, n = 14. B) Non-Weight-Matched (NWM), T1, n = 23; T2, n = 52; T3, n = 33. Error bars represent SD

Discussion

The purpose of this cross-sectional study was, to compare the inter-individual thermoregulatory and cardiovascular responses to weight-bearing exercise in pregnant women. To make our comparison, we examined weight-matched and non-weight matched groups across pregnancy timepoints (T1, T2 & T3) to differentiate the role of total body weight and pregnancy timepoint on these responses. We observed a similar sum and rate of H_{prod}, HR, and RPE at baseline and during exercise in pregnant women of the same total body mass (i.e., ~71 kg) between early (T1) to middle (T2) and late (T3) pregnancy timepoints. On the other hand, in our NWM group with greater total body weight from T1(~65 kg), T2 (~75 kg) to T3 (~80 kg), the sum and rate of H_{prod}, and HR increased between pregnancy-timepoints at baseline and during the incremental weight-bearing exercise protocol. With this novel design (i.e., inclusion of a WM group), it was possible to differentiate the role of total body weight and pregnancy timepoint on the sum and rate of H_{prod}, HR and RPE responses.

Although thermoregulatory function during exercise has been extensively studied in pregnancy, the influence of weight gain during pregnancy on H_{prod} and, subsequently, thermoregulatory responses during exercise remained equivocal (Jones *et al.*, 1985; McMurray *et al.*, 1993; Lindqvist *et al.*, 2003; Soultanakis-Aligianni, 2003; Soultanakis, 2016). For instance, a common practice used when evaluating thermoregulatory responses was to compare women from early, middle to late pregnancy during weight-bearing exercise at a given exercise intensity (i.e., different speed/incline and/or %VO_{2peak}) (Jones *et al.*, 1985; McMurray *et al.*, 1993; Lindqvist *et al.*, 2003). Such a design confounds thermoregulatory responses because of differences in body weight from early, middle to late pregnancy, and varying heat production from exercise. Therefore, heat loss (e.g., skin blood flow and evaporation of sweat) will respond according to weight and level of heat production. To our knowledge, no study had been designed to evaluate H_{prod} in weight-matched pregnant women throughout pregnancy. It is important to mention that the women from the present study assessed in T1, T2, and T3 for both the WM and NWM groups presented similar GWG relative to the upper limit of the recommended weight gain for their gestational week. Moreover, physical activity levels were similar for both experimental groups at each pregnancy timepoint. The lack of significant between-group differences minimize the potential impact of the level of physical activity and GWG, two factors known to influence physiological and perceptual responses to exercise (Carpenter *et al.*, 1990; Pivarnik *et al.*, 1991; Pivarnik, 1994; Mottola *et al.*, 2006; Dobson *et al.*, 2020). Weight gain as pregnancy progresses is characterized by a multitude of physiological changes such as elevated systemic cardiovascular function (i.e., increased blood volume, cardiac output, vascular resistance) (Carbillon *et al.*, 2000; Desai *et al.*, 2004; San-Frutos *et al.*, 2011), anatomical and respiratory changes (i.e., reduced functional residual capacity, decreased lung capacity) (Hegewald & Crapo, 2011) and endocrine adaptations (i.e., increased gonadoptrophin-releasing and corticortrophin hormones increase) (Petraglia *et al.*, 1992) to accommodate a growing fetus. Sympathetic nervous system activity seems to increase across gestation, explaining the increased resting HR in pregnant women (Purdy *et al.*, 2019). In the present study, HR demonstrated the same trends as H_{prod} during exercise in both WM and NWM groups. This outcome was expected considering previous findings from the literature (Knuttgen & Emerson, 1974; Pernoll *et al.*, 1975; Desai *et al.*, 2004). The method of comparing timepoint of pregnancy without accounting for total body weight often resulted in a greater increase in VO_2 and HR across pregnancy compared to non-pregnant women due to the large differences in total body weight (Knuttgen & Emerson, 1974; Pernoll *et al.*, 1975; Carpenter *et al.*, 1990).

A recent study by our group (Dobson *et al.*, 2020) compared RPE among other physiological variables (i.e., HR and VO_2) throughout pregnancy in a subset of these same women during submaximal weight-bearing exercise to determine predictors of its responses during submaximal exercise. The authors reported RPE significantly increased from early- to late-pregnancy (Dobson *et al.*, 2020). In the current study, although RPE had the same results as the physiological markers assessed for the WM group, it was the only variable that did not increase across pregnancy in the NWM group. The design differences between our study and Dobson *et al.*, 2020 might have contributed to the disparate outcomes, as our study used an inter-group comparison, whereas Dobson *et al.*, 2020 used an intra-group analysis (i.e., same women evaluated at different pregnancy timepoints) (Dobson *et al.*, 2020). The relationship between RPE, pregnancy, and GWG may have different variables contributing to the inconsistencies in the literature. For example, Wolfe and Weissgerber (2003) suggested that an increased RPE is a result of GWG during weight-bearing activities (Wolfe & Weissgerber, 2003), while others have observed a decrease in RPE for a fixed exercise intensity from early to late pregnancy (Pivarnik *et al.*, 1991). Another possible explanation is that physical activity levels influence RPE responses to exercise (Dobson *et al.*, 2020), and since there were no differences in physical activity level in groups across pregnancy timepoints (which would not be the case if the design was longitudinal), this could potentially explain the maintenance of RPE across pregnancy in the NWM group.

The present study has limitations. We did not have measurements and could not account for fat-mass and fat-free mass when comparing between the WM and NWM groups. Since weight was higher in T3 vs. T2, vs. T1 in the NWM the proportion of fat-mass and fat-free mass may have been different and may have contributed to the variability in both baseline and exercise-related H_{prod} across pregnancy (Petrella *et al.*, 2014; Most *et al.*, 2018). In addition, our findings cannot be directly translated to younger (e.g., adolescents) or older women (i.e., >40 years old), and may not apply to those with pregnancy-related health issues, such as preeclampsia or gestational diabetes. Further studies can help elucidate these aspects. In terms of strengths, the present study outcomes have important implications for designing experiments directed at evaluating thermoregulatory function in pregnant women and provide valuable insight into the contribution of total body weight in H_{prod}. The observed similar H_{prod} during incremental weight-bearing exercise for weight-matched participants between pregnancy timepoints confirm that this design may be important for mechanistic research on thermoregulatory function. Besides including H_{prod}, our study also incorporated other physiological (i.e., HR) and perceptual (i.e., RPE) markers. Finally, we were able to account for GWG classification as a percentage of the upper limit recommended for an individual's gestational age as well as physical activity measured by accelerometer.

Conclusion

The present study was designed to provide what is believed to be the first evaluation of H_{prod} during rest and an incremental exercise protocol across three distinct pregnancy timepoints, matched for total body weight. By comparing groups of similar weight to those with increasing body weight with progressing pregnancy timepoints, we demonstrated that if total body weight held constant, H_{prod} will respond accordingly. Despite the long-standing belief that pregnancy timepoint was the driving force in thermoregulatory responses during exercise, our results indicate that total body weight separate from pregnancy timepoint is a crucial modulator in H_{prod} during exercise at a fixed intensity.

AUTHOR CONTRIBUTION

The authors have seen and approved the manuscript.

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References

Borg, G. A. (1982). Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*, *14*(5), 377-381.

Breithaupt, P., Adamo, K. B., & Colley, R. C. (2012). The HALO submaximal treadmill protocol to measure cardiorespiratory fitness in obese children and youth: a proof of principle study. *Appl Physiol Nutr Metab*, *37*(2), 308-314. doi:10.1139/h2012-003

Carbillon, L., Uzan, M., & Uzan, S. (2000). Pregnancy, vascular tone, and maternal hemodynamics: a crucial adaptation. *Obstet Gynecol Surv*, *55*(9), 574-581. doi:10.1097/00006254-200009000-00023

Carpenter, M. W., Sady, S. P., Sady, M. A., Haydon, B., Coustan, D. R., & Thompson, P. D. (1990). Effect of maternal weight gain during pregnancy on exercise performance. *J Appl Physiol (1985), 68*(3), 1173-1176. doi:10.1152/jappl.1990.68.3.1173

Clapp, J. F., 3rd. (1991). The changing thermal response to endurance exercise during pregnancy. *Am J Obstet Gynecol*, *165*(6 Pt 1), 1684-1689. doi:10.1016/0002-9378(91)90015-j

Clapp, J. F., 3rd, Wesley, M., & Sleamaker, R. H. (1987). Thermoregulatory and metabolic responses to jogging prior to and during pregnancy. *Med Sci Sports Exerc*, *19*(2), 124-130.

Clarke, P. E., & Gross, H. (2004). Women's behaviour, beliefs and information sources about physical exercise in pregnancy. *Midwifery, 20*(2), 133-141.doi:10.1016/j.midw.2003.11.003

Colley, R., Connor Gorber, S., & Tremblay, M. S. (2010). Quality control and data reduction procedures for accelerometry-derived measures of physical activity. *Health Rep*, *21*(1), 63-69.

Davenport, M. H., Ruchat, S. M., Poitras, V. J., Jaramillo Garcia, A., Gray, C. E., Barrowman, N., . . . Mottola, M. F. (2018). Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. *Br J Sports Med*, *52*(21), 1367-1375. doi:10.1136/bjsports-2018-099355

Desai, D. K., Moodley, J., & Naidoo, D. P. (2004). Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. *Obstet Gynecol, 104*(1), 20-29. doi:10.1097/01.AOG.0000128170.15161.1d

da Silva, D.F., Mohammad, S., Hutchinson, K. A., & Adamo, K. B. (2020). Cross-Validation of Ratings of Perceived Exertion Derived from Heart Rate Target Ranges Recommended for Pregnant Women. *Int J Exerc Sci, 13*(3), 1340-1351.

Dobson, K. L., da Silva, D. F., Dervis, S., Mohammad, S., Nagpal, T. S., & Adamo, K. B. (2020). Physical activity and gestational weight gain predict physiological and perceptual responses to exercise during pregnancy. *Birth Defects Res*. doi:10.1002/bdr2.1808

Franklin, A., Mishtal, J., Johnson, T., & Simms-Cendan, J. (2017). Rowers' Self-Reported Behaviors, Attitudes, and Safety Concerns Related to Exercise, Training, and Competition During Pregnancy. *Cureus, 9*(8), e1534-e1534. doi:10.7759/cureus.1534

Graham, J. M., Jr., Edwards, M. J., & Edwards, M. J. (1998). Teratogen update: gestational effects of maternal hyperthermia due to febrile illnesses and resultant patterns of defects in humans. *Teratology, 58*(5), 209-221. doi:10.1002/(sici)1096 9926(199811)58:5<209::Aid-tera8>3.0.Co;2-q

Hartgill, T. W., Bergersen, T. K., & Pirhonen, J. (2011). Core body temperature and the thermoneutral zone: a longitudinal study of normal human pregnancy. *Acta Physiol (Oxf), 201*(4), 467-474. doi:10.1111/j.1748-1716.2010.02228.x

Hartmann, S., & Bung, P. (1999). Physical exercise during pregnancy-physiological considerations and recommendations. *J Perinat Med, 27*(3), 204-215. doi:10.1515/jpm.1999.029

Havenith, G., Coenen, J. M., Kistemaker, L., & Kenney, W. L. (1998). Relevance of individual characteristics for human heat stress response is dependent on exercise intensity and climate type. *Eur J Appl Physiol Occup Physiol, 77*(3), 231-241. doi:10.1007/s004210050327

Hegewald, M. J., & Crapo, R. O. (2011). Respiratory physiology in pregnancy. *Clin Chest Med, 32*(1), 1-13. doi:10.1016/j.ccm.2010.11.001

Institute of, M., & National Research Council Committee to Reexamine, I. O. M. P. W. G. (2009). The National Academies Collection: Reports funded by National Institutes of Health. In K. M. Rasmussen & A. L. Yaktine (Eds.), *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington (DC): National Academies Press (US) Copyright © 2009, National Academy of Sciences.

Jones, R. L., Botti, J. J., Anderson, W. M., & Bennett, N. L. (1985). Thermoregulation during aerobic exercise in pregnancy. *Obstet Gynecol, 65*(3), 340-345.

Knuttgen, H. G., & Emerson, K., Jr. (1974). Physiological response to pregnancy at rest and during exercise. *J Appl Physiol, 36*(5), 549-553. doi:10.1152/jappl.1974.36.5.549

Lindqvist, P. G., Marsal, K., Merlo, J., & Pirhonen, J. P. (2003). Thermal response to submaximal exercise before, during and after pregnancy: a longitudinal study. *J Matern Fetal Neonatal Med, 13*(3), 152-156. doi:10.1080/jmf.13.3.152.156

McMurray, R. G., Katz, V. L., Meyer-Goodwin, W. E., & Cefalo, R. C. (1993). Thermoregulation of pregnant women during aerobic exercise on land and in the water. *Am J Perinatol, 10*(2), 178-182. doi:10.1055/s-2007-994656

Medek, H., Halldorsson, T., Gunnarsdottir, I., & Geirsson, R. T. (2016). Physical activity of relatively high intensity in mid-pregnancy predicts lower glucose tolerance levels. *Acta Obstet Gynecol Scand, 95*(9), 1055-1062. doi:10.1111/aogs.12931

Metcalfe, J., & Ueland, K. (1974). Maternal cardiovascular adjustments to pregnancy. *Prog Cardiovasc Dis, 16*(4), 363-374. doi:10.1016/0033-0620(74)90028-0

Miller, M. W., Nyborg, W. L., Dewey, W. C., Edwards, M. J., Abramowicz, J. S., & Brayman, A. A. (2002). Hyperthermic teratogenicity, thermal dose and diagnostic ultrasound during pregnancy: implications of new standards on tissue heating. *Int J Hyperthermia, 18*(5), 361-384. doi:10.1080/02656730210146890

Most, J., Marlatt, K. L., Altazan, A. D., & Redman, L. M. (2018). Advances in assessing body composition during pregnancy. *Eur J Clin Nutr, 72*(5), 645-656. doi:10.1038/s41430-018-0152-8

Mottola, M. F., Davenport, M. H., Brun, C. R., Inglis, S. D., Charlesworth, S., & Sopper, M. M. (2006). VO2peak prediction and exercise prescription for pregnant women. *Med Sci Sports Exerc, 38*(8), 1389-1395. doi:10.1249/01.mss.0000228940.09411.9c

Mottola, M. F., Davenport, M. H., Ruchat, S. M., Davies, G. A., Poitras, V. J., Gray, C. E., Zehr, L. (2018). 2019 Canadian guideline for physical activity throughout pregnancy. *Br J Sports Med, 52*(21), 1339-1346. doi:10.1136/bjsports-2018-100056

Nascimento, S. L., Surita, F. G., & Cecatti, J. G. (2012). Physical exercise during pregnancy: a systematic review. *Curr Opin Obstet Gynecol, 24*(6), 387-394. doi:10.1097/GCO.0b013e328359f131

Nielsen, B., & Davies, C. T. (1976). Temperature regulation during exercise in water and air. *Acta Physiol Scand, 98*(4), 500-508. doi:10.1111/j.1748-1716.1976.tb10342.x

Pernoll, M. L., Metcalfe, J., Schlenker, T. L., Welch, J. E., & Matsumoto, J. A. (1975). Oxygen consumption at rest and during exercise in pregnancy. *Respir Physiol, 25*(3), 285-293. doi:10.1016/0034-5687(75)90004-3

Petraglia, F., Woodruff, T. K., Botticelli, G., Botticelli, A., Genazzani, A. R., Mayo, K. E., & Vale, W. (1992). Gonadotropin-releasing hormone, inhibin, and activin in human placenta: evidence for a common cellular localization. *J Clin Endocrinol Metab, 74*(5), 1184-1188. doi:10.1210/jcem.74.5.1569165

Petrella, E., Malavolti, M., Bertarini, V., Pignatti, L., Neri, I., Battistini, N. C., & Facchinetti, F. (2014). Gestational weight gain in overweight and obese women enrolled in a healthy lifestyle and eating habits program. *J Matern Fetal Neonatal Med, 27*(13), 1348-1352. doi:10.3109/14767058.2013.858318

Physical Activity and Exercise During Pregnancy and the Postpartum Period: ACOG Committee Opinion, Number 804. (2020). *Obstet Gynecol, 135*(4), e178-e188. doi:10.1097/aog.0000000000003772

Pivarnik, J. M. (1994). Maternal exercise during pregnancy. *Sports Med, 18*(4), 215-217. doi:10.2165/00007256-199418040-00001

Pivarnik, J. M., Lee, W., & Miller, J. F. (1991). Physiological and perceptual responses to cycle and treadmill exercise during pregnancy. *Med Sci Sports Exerc, 23*(4), 470-475.

Purdy, G. M., James, M. A., Wakefield, P. K., Skow, R. J., Van Diepen, S., May, L. E., .Steinback, C. D. (2019). Maternal cardioautonomic responses during and following exercise throughout pregnancy. *Appl Physiol Nutr Metab, 44*(3), 263-270. doi:10.1139/apnm-2018-0397

San-Frutos, L., Engels, V., Zapardiel, I., Perez-Medina, T., Almagro-Martinez, J., Fernandez, R., & Bajo-Arenas, J. M. (2011). Hemodynamic changes during pregnancy and postpartum: a prospective study using thoracic electrical bioimpedance. *J Matern Fetal Neonatal Med, 24*(11), 1333-1340. doi:10.3109/14767058.2011.556203

Soultanakis-Aligianni, H. N. (2003). Thermoregulation during exercise in pregnancy. *Clin Obstet Gynecol, 46*(2), 442-455. doi:10.1097/00003081-200306000-00023

Soultanakis, H. N. (2016). Aquatic Exercise and Thermoregulation in Pregnancy. *Clin Obstet Gynecol, 59*(3), 576-590. doi:10.1097/grf.0000000000000209

Spatling, L., Fallenstein, F., Huch, A., Huch, R., & Rooth, G. (1992). The variability of cardiopulmonary adaptation to pregnancy at rest and during exercise. *Br J Obstet Gynaecol, 99 Suppl 8*, 1-40.

Szymanski, L. M., & Kogutt, B. K. (2018). Uterine Artery Doppler Velocimetry During Individually Prescribed Exercise in Pregnancy. *Obstet Gynecol, 132*(4), 1026-1032. doi:10.1097/aog.0000000000002779

Tan, E. K., & Tan, E. L. (2013). Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol, 27*(6), 791-802. doi:10.1016/j.bpobgyn.2013.08.001

Vähä-Eskeli, K., Erkkola, R., & Seppänen, A. (1991). Is the heat dissipating ability enhanced during pregnancy? *Eur J Obstet Gynecol Reprod Biol, 39*(3), 169-174. doi:10.1016/0028-2243(91)90053-n

Wolfe, L. A., & Weissgerber, T. L. (2003). Clinical physiology of exercise in pregnancy: a literature review. *J Obstet Gynaecol Can, 25*(6), 473-483. doi:10.1016/s1701-2163(16)30309-7

CHAPTER 5

PREAMBLE TO ARTICLE 3

Study 2 established that, when examining heat production during exercise in pregnancy, it is necessary to account for body weight in the experimental design. However, we must also consider the other side of the heat balance equation − heat loss. Accordingly, this chapter provides a scoping review of the current literature on heat loss mechanisms throughout pregnancy. This study outlines what is currently available in the literature regarding experimental design and measurements in pregnant women regarding evaporative and dry heat loss mechanisms. The following study titled "Heat loss responses at rest and during exercise in pregnancy: A scoping review." is presented in Chapter 5. This article is in revision with the Journal of Thermal Biology (March 2020).

Title:

Heat loss responses at rest and during exercise in pregnancy: A scoping review.

Authors:

Sheila Dervis[a], Kayla Lerher Dobson[a], Taniya Singh Nagpal[a], Carla Geurts[a], François Haman[a], Kristi Bree Adamo[a]

Author Affiliations:

[a] Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, Ottawa, ON, Canada, K1N 6N5.

Corresponding Author:

Dr. Kristi B. Adamo

Associate Professor

School of Human Kinetics, Faculty of Health Sciences

Lees Campus, E 250F

200 Lees Ave. Ottawa, ON K1N 6N5

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Abstract

Background: The teratogenic risk associated with maternal hyperthermia has been a crucial motive in understanding thermoregulatory responses in pregnancy. Studies have focused on core temperature responses in a wide range of exercise intensities, duration, and ambient temperatures. Fortunately, none have reported core temperatures exceeding 39.0°C. Nonetheless, there are limited studies that have provided substantial insight into both dry and evaporative heat loss mechanisms that are involved in facilitating the maintenance of core temperature (≥39.0°C) during heat stress in pregnant women. The purpose of this scoping review was to summarize the available literature that has assessed heat loss responses in studies of human pregnancy.

Methods: A search strategy was developed combining the terms pregnancy, thermoregulation, and adaptation. A systematic search was performed in the following databases: PubMed, Embase, Scopus, and ProQuest. Studies eligible for inclusion examined pregnant women between the ages of 18-40 years old and measured at least one of the following: sweating, blood flow, skin temperature, or behavioural responses to heat stress or exercise. Retrieved data were categorized as evaporative (sweating), dry or behavioural heat loss responses and were summarized narratively.

Results: Thirty-three studies were included (twenty-nine measured physiological responses and four measured behavioural responses). Studies suggest that evaporative (sweating) and dry (skin blood flow and temperature) heat loss responses increase from early to late pregnancy at rest and during exercise due to a systemic drive (i.e., greater cardiac output, blood volume and reduced vascular resistance). Behavioural heat loss responses are also influenced by cultural/religious expectations, personal preferences and sociodemographic.

Conclusion: The findings suggest that pregnancy modifies evaporative (sweating), dry and behavioural heat loss responses. However, there is an opportunity for future studies to compare heat loss accounting for gestational weight gain and use tools like a thermal sensation/comfort scale to associate physiological responses with perceptual responses across pregnancy.

Keywords: Pregnancy, thermoregulation, behavioural adaptation.

1.0 Introduction

There has been a gradual evolution in popular medical opinion regarding the maintenance of a healthful pregnancy; from the prescription of being sedentary in the late nineteenth/early twentieth century, to more modern, evidence-informed support of an active pregnancy. Current prenatal advice encourages women to continue their same occupational tasks, and activities of daily living, as well as follow physical activity guidelines (2002; Davies *et al.*, 2003b; Davenport *et al.*, 2018a; Mottola *et al.*, 2018b). In the absence of contraindications described in detail in a review by Evenson *et al* (Evenson *et al.*, 2014), following prenatal physical activity recommendations is associated with maternal health benefits, including improved management of gestational weight gain, a lower risk of preeclampsia and gestational hypertension, and fewer newborn complications (Davenport *et al.*, 2018b; Ruchat *et al.*, 2018; Davenport *et al.*, 2019a; Davenport *et al.*, 2019b). Despite the growing evidence supporting physical activity throughout gestation, a perceived barrier pregnant women have is fear of compromised maternal-fetal wellbeing due to overexertion or overheating associated with exercise (Franklin *et al.*, 2017b). The concerns surrounding heat-related injury illustrates the need for more evidence-based research examining exercise or heat stress in pregnancy. The teratogenic risks associated with maternal hyperthermia (i.e., core temperature ≥39.0°C) are comparable to most healthy adults. Thus, individuals are recommended to avoid excessive heat stress (e.g., from extreme exercise and/or passive heat exposure), preventing heat related injuries (e.g., heat stroke) (Graham *et al.*, 1998; Miller *et al.*, 2002). Fortunately, there have been extensive reviews regarding maternal core temperature response under various thermal stress and exercise intensities (McMurray & Katz, 1990; Katz, 1996; Soultanakis-Aligianni, 2003; Ziskin & Morrissey, 2011; Soultanakis, 2016; Ravanelli *et al.*, 2019). No published studies that have assessed core temperatures of pregnant women during exercise or passive heat exposure have reported a value exceeding the teratogenic limit. (Jones *et al.*, 1985; Clapp *et al.*, 1987; McMurray *et al.*, 1990; Clapp, 1991; Vaha-Eskeli *et al.*, 1991; McMurray *et al.*, 1993; O'Neill, 1996; Lindqvist *et al.*, 2003; Larsson & Lindqvist, 2005; Clapp, 2006; Tuffnell *et al.*, 2009; Brearley *et al.*, 2015; Petrov Fieril *et al.*, 2016a).

The cardiovascular shifts that occur during pregnancy are key modulators of the body's capacity to dissipate heat (Clapp *et al.*, 1987; Clapp, 1991; McMurray *et al.*, 1993; Hartmann & Bung, 1999; Hartgill *et al.*, 2011; Soultanakis, 2016; Ravanelli *et al.*, 2019). Plasma and blood volume slowly increase by 40-50% throughout pregnancy to accommodate the developing fetus, increasing the heart rate (15 beats/min more than usual), stroke volume, and cardiac output (Spatling *et al.*, 1992; Hartmann & Bung, 1999). Systemic vascular resistance also drops due to smooth muscle relaxation and overall vasodilation caused by elevated progesterone, leading to a fall in blood pressure (Hartmann & Bung, 1999). Increases in blood flow appear to counteract the elevation of heat storage *via* dry heat loss (i.e., skin blood flow and skin temperature) (Metcalfe & Ueland, 1974; Spatling *et al.*, 1992; Hartmann & Bung, 1999; Ravanelli *et al.*, 2019). Throughout pregnancy, heat transfer between mother and fetus occurs predominantly *via* the placental wall and uterine blood flow (Ziskin & Morrissey, 2011). In circumstances when maternal core temperature increases, there is evidence of reduced uterine blood flow (Clapp, 1980; Chandler & Bell, 1981), although maternal-fetal protective mechanisms exist to preserve nutrient supply to the fetus (Curet *et al.*, 1976; Lotgering *et al.*, 1983; Clapp, 2006). Fetal heat balance is maintained by a temperature difference of ~0.5°C greater in fetus compared to mother, and most of the heat dissipation occurs via convective cooling in umbilical and placental blood circulation (Power, 1989; Schröder & Power, 1997; Asakura, 2004) while ~15% happens through conductive cooling via amniotic fluids (Asakura, 2004). Therefore, fetal heat balance is entirely dependent upon maternal temperature as well as circulation (convection) to prevent hyperthermia (Ziskin & Morrissey, 2011). However, many of the findings used to understand heat loss mechanisms in pregnancy are derived from animal studies (Curet *et al.*, 1976; Clapp, 1980; Chandler & Bell, 1981; Lotgering *et al.*, 1983; Power, 1989; Schröder & Power, 1994; Edwards *et al.*, 2003). Extrapolating the findings of animal studies to humans in terms of absolute core temperature is inappropriate, since resting core temperature of animals (e.g., sheep ~39°C, birds ~40-42 °C, and rats ~38.5°C) (Prozesky, 1963; Baker *et al.*, 1979; Edwards *et al.*, 2003) is often not the same as humans (~37°C). The most effective thermo-effector response to heat stress in humans is the evaporation of sweat, which, in many animals is not physiologically possible (Robertshaw, 2006). For example, rodents depend more on increased metabolic rate while humans rely initially on vasomotor control of sweating and peripheral circulation (Havenith, 2005; Hankenson *et al.*, 2018). Hence, a direct thermoregulatory comparison between humans and animals presents a challenge in both heat loss responses and the broader physiological range in absolute core temperature in animals.

When environmental temperatures exceed body temperature, mammals must rely on physiological and behavioural responses to either reduce heat load or increase heat loss and ultimately achieve heat balance (Mitchell *et al.*, 2018; McFarland *et al.*, 2019). Behavioural responses to heat stress exposure in animals compare to humans, for example, it has been observed that primates will avoid physical exertion and spend more time resting (Campos & Fedigan, 2009; Majolo *et al.*, 2013), seek out cool areas (Stelzner & Hausfater, 1986; Barrett *et al.*, 2004; Duncan & Pillay, 2013), or modify physical postures that are conducive to heat dissipation (Stelzner & Hausfater, 1986; Bicca-Marques & Calegaro-Marques, 1998; Campos & Fedigan, 2009). Various human studies using different thermal scales (e.g., thermal comfort and/or thermal sensation scales) evaluating subjective responses to changes in ambient temperature have indicated that females are more sensitive than males to a deviation from a comfortable temperature (Cena & de Dear, 2001; Pellerin & Candas, 2003; Karjalainen, 2012; Kingma *et al.*, 2012; Schellen *et al.*, 2012). As such, when ambient environmental conditions change (to either warm or cool conditions), females might demonstrate modifications in thermoregulatory behaviour sooner than their male counterparts. However, behavioural thermoregulatory responses (e.g., seeking shade, altering/removing clothing, modifying chores) associated with a greater perceptual sensitivity during pregnancy may be affected by a combination of personal preferences (Downey, 2008), cultural values, religion, and physical or social environments (Ejidokun, 2000; Downey, 2008; Basu *et al.*, 2010; Wulandari & Klinken Whelan, 2011; Ngongalah *et al.*, 2018). The combination of behaviours driven by perceptual and cultural/religious responses play a crucial role in pregnancy and have yet to be studied.

The primary aim of this scoping review is to identify human studies that measured physiological (i.e., sweating, cardiovascular system/blood flow and skin temperature) and behavioural/cultural heat loss responses across pregnancy, then to characterize the results based on exercise or passive heat exposure. Given the disparate findings in human studies regarding heat loss responses specifically throughout pregnancy, a scoping review was deemed appropriate to map findings and inform research gaps that can be addressed in future investigations.

2.0 Methods

A scoping review was performed to assess the available literature on heat loss mechanisms in pregnancy, following the Arksey and O'Malley (Arksey & O'Malley, 2005) framework, and the Peters *et al.* (Peters *et al.*, 2020) PRISMA-ScR checklist was completed (Table 2). The review focused on human studies and pertinent heat loss mechanisms during exercise and passive heat exposure in pregnancy. The studies are characterized based on quantitative measurements (e.g., skin blood flow, sweating, and skin temperature) and qualitative measurements (e.g., behaviour, cultural and socioeconomic responses) of heat loss across all pregnancy stages.

2.1 Inclusion & Exclusion Criteria

This scoping review comprised women between the ages of 18 and 40 years. The population group included women of different pregnancy stages both healthy and compromised health status (e.g., preeclampsia) and/or non-pregnant. The thermoregulatory measurements contained at least one behavioural/perceptual/cultural and/or physiological heat loss variable, including sweating, skin blood flow, systemic blood flow, skin temperature, and/or cardiovascular responses. To test the range of thermoregulatory function in pregnancy, many studies included a variety of thermal stress conditions, such as different exercises and passive heat exposures (i.e., saunas, hot tubs, thermal chambers etc.). Studies were excluded if measurements were based on animal studies, review articles, case studies, editorials, book chapters, and commentaries. However, reference lists of relevant reviews were scanned for potential eligible studies that met our inclusion criteria. Considering the available results, outcomes may suggest further investigation on this topic.

2.2 Search Strategy and Screening

The search strategy and terms are outlined in Table 1. The key terms were searched in the following databases from September 2020: PUBMED, EMBASE, SCOPUS and PROQUEST (for grey literature, specifically theses and dissertations) was undertaken followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A date restriction was not applied. A second search using all identified keywords and index terms was undertaken across all included databases. The retrieved articles were transferred to COVIDENCE, and the automatic duplicate removal feature was used. Two reviewers (SD and KLD) independently screened titles/abstracts, and eligible studies then were reviewed in full text.

2.3 Data Extraction and synthesis

Data from the eligible studies were charted on a standard excel spreadsheet. One independent reviewer finalized the charting (SD) and the other reviewer (KLD) completed a quality check for ten included studies at random. The following study characteristics were extracted: country of study, total sample size, description of methods, heat loss measurements, and main findings related to research question. The main findings from included studies informed the outcomes of physiological heat loss (i.e., sweating, cardiovascular system/blood flow and skin temperature) and behavioural/cultural responses in pregnant women. The findings are presented using diagrams, tables, and/or descriptive format that aligns with the objectives of this review. Data were analyzed narratively by summarizing the main findings in heat loss measurements in human studies.

Table 1. Outline of Medline Search

Heading	Search Strategy
Pregnancy	(Pregnancy) OR (gestation)) OR (perinatal)) OR (pregnant)
Thermoregulation	(Thermoregulation) OR (temperature)) OR (core temperature)) OR (body temperature)) OR (skin temperature)) OR (thermal response)) OR (sweating)) OR (heat loss) OR (heat dissipation)) OR (skin blood flow)) OR (blood flow)
Adaptation	(Thermal behaviour)) OR (thermal adaptation) OR (cultural adaptation) OR (social adaptation))
	Above searches combined with AND

Table 2. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.

Section	Item	PRISMA-ScR CHECKLIST ITEM	Reported on Page #
TITLE			
Title	1	Identify the report as a scoping review	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5
METHODS			
Protocol and Registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6

Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	6
Information sources	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	7
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	7
Selection of sources of evidence	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	7
Data charting process	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	7
Critical appraisal of individual sources of evidence	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	10
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	10

Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	18
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	18
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	27
Limitations	20	Discuss the limitations of the scoping review process.	32
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	34
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	N/A

3.0 Results

A total of 297 articles were identified from the research databases, and after removing duplicates, 211 titles and abstracts were screened. Of the identified articles, 81 full-text articles were further assessed for eligibility, and 33 were included in the final synthesis. A flow chart (i.e., PRISMA flow diagram) for study inclusion and exclusion is presented in Figure 1. Of the 33 studies included in this review, 12 were from the United States of America, 3 from Finland, 2 from each of the United Kingdom, Switzerland, Norway, and Sweden and 1 from each of Brazil, Slovenia, Canada, Germany, Spain, Portugal, Australia, Israel, Nigeria, and Indonesia. Fourteen studies were quantitative experimental, ten were longitudinal in design, three were randomized control clinical trials, and one from each, case-crossover, randomized case-crossover, qualitative grounded theory, qualitative descriptive, prospective cross-sectional, and qualitative mixed methods. Table 3 includes a description of study characteristics.

3.1 Summary of heat loss in sweating and weight change in pregnancy

The limited studies (Jones *et al.*, 1985; Clapp, 1991; McMurray *et al.*, 1993; Dunlap, 2003) measuring sweat losses during exercise or heat stress in human pregnancies provide preliminary evidence that physiological thermal protective changes occur throughout pregnancy. A longitudinal study (Jones *et al.*, 1985) focused on thermoregulatory function during exercise in active pregnant women. The authors followed 4 physically active women throughout pregnancy, measured rectal/skin temperatures and sweat losses calculated as a change in body weight corrected for respiratory contribution before and after weight-bearing exercise at about 80-90% VO_{2peak}, (Jones *et al.*, 1985). The resting rectal temperature decreased as pregnancy progressed, however, external work (kcal) increased resulting in similar end-exercise sweat production (Jones *et al.*, 1985). A comparable study (Clapp, 1991) that assessed thermoregulatory responses to weight bearing exercise (i.e., running) followed 18 physically active pregnant women, the authors ensured participants who maintained exercise equating to 64% VO_{2peak} before conception, treadmill was set at a consistent speed/grade and this intensity followed through to late pregnancy. The onset of sweating was measured subjectively, with participants indicating the moment at which they 'felt' sweating start and the associated core temperature was recorded at that time (i.e., thermo-sensitivity) (Clapp, 1991). The authors reported the rectal temperature at which sweating began during exercise decreased at a rate of ~0.08°C per month of gestation, and heat loss responses to exercise improved from early to late pregnancy (Clapp, 1991).

A randomized case cross-over study (McMurray *et al.*, 1993) in 7 healthy pregnant women evaluated thermoregulatory responses during exercise on land and in the water at comparable intensities. Exercise protocols were both non-weight bearing cycling at 70% maternal heart rate, researchers estimated evaporative heat loss (E) based on weight change, using the following equation: E = weight loss (g)*2.43 kJ/gm (McMurray *et al.*, 1993). Although, metabolic rate was similar in both land and water exercise, there was greater heat storage (kJ/hour) and heat loss (kJ/hour) on land (McMurray *et al.*, 1993). A comparable study in 12 healthy pregnant women by Dunlap *et al* (Dunlap, 2003) , examined total body sweat loss responses pre- and post- resting at baseline, during structured aerobic exercise class and recovery inside either a 27.7 or 33.5°C pool. Although the metabolic rate ($mL\cdot kg^{-1}\cdot min^{-1}$) was similar in both pools, the total body sweat losses (kg) was greater in the warmer (33.5°C) pool (Dunlap, 2003). Available thermoregulation studies during pregnancy demonstrate that physiological responses protect women from hyperthermia, even when exercising at submaximal intensity in adverse environments (i.e., warmer pool at 33.5°C) (Dunlap, 2003).

3.2 Summary of dry heat loss responses in blood flow and skin temperature in pregnancy

Most studies measuring dry heat loss or blood flow in pregnant women examined either systemic (Moore *et al.*, 1988; Pivarnik *et al.*, 1990; Vähä-Eskeli *et al.*, 1991b; Erkkola *et al.*, 1992; Macaulay *et al.*, 1992; Clapp & Capeless, 1997; Chapman *et al.*, 1998; Clapp *et al.*, 2000; Jeffreys *et al.*, 2006; Baciuk *et al.*, 2008; Salvesen *et al.*, 2012; Szymanski & Kogutt, 2018) (i.e., cardiac output, stroke volume, blood volume, uterine/splanchnic blood flow and umbilical blood flow and systemic vascular resistance) and/or peripheral (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Jones *et al.*, 1985; Beinder *et al.*, 1990; Vähä-Eskeli *et al.*, 1991a; Tur *et al.*, 1992a; McMurray *et al.*, 1993; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Stark *et al.*, 2006; Baciuk *et al.*, 2008; Cankar *et al.*, 2010; Hartgill *et al.*, 2011; Sillero-Quintana *et al.*, 2012; Simoes *et al.*, 2012; Iacobaeus *et al.*, 2017) (i.e., skin blood flow, peripheral skin vasoconstriction/vasodilation and skin temperature) responses at rest, during passive heat exposure and/or exercise. The prevailing responses in systemic cardiovascular remodeling that occurs across pregnancy (Pivarnik *et al.*, 1990; Clapp & Capeless, 1997; Chapman *et al.*, 1998) have demonstrated that the changes begin early and progress as pregnancy advances (Pivarnik *et al.*, 1990; Vähä-Eskeli *et al.*, 1991b; Clapp & Capeless, 1997). Overall, from early to late stages of pregnancy, there is an absolute rise in cardiac output (L/min) and stroke volume (mL) and decrease in vascular resistance persists until term and may in some cases remain several weeks into post-partum (Pivarnik *et al.*, 1990; Vähä-Eskeli *et al.*, 1991b; Clapp & Capeless, 1997).

During pregnancy, blood flow to the uterus and placenta represents up to ~25% of cardiac output and is essential for the developing fetus (Newton & May, 2017). When moderate maternal stress from exercise results in visceral blood flow redistribution, placental perfusion is maintained due to increased cardiac output (Newton & May, 2017). Szymanski *et al* (Szymanski & Kogutt,

2018) evaluated uterine artery blood flow using ultrasound Doppler measurements in pregnant women in response to exercise performed at moderate intensity according to the American College of Obstetricians and Gynecologists standards (2002). The authors reported that engaging in PA at the recommended intensity did not reduce uterine artery blood flow or adversely affect fetal well-being in physically active and non-active pregnant women (Szymanski & Kogutt, 2018). Furthermore, measurements of uteroplacental blood flow with Doppler ultrasound was assessed during and after incremental treadmill running, starting with a low intensity warm-up, and building up to vigorous intensity exercise in pregnant elite athletes (Salvesen *et al.*, 2012). The mean uterine artery volume flow decreased by ~60-80% from the initial value after warming up. Throughout most of the series of exercise intensity increments, uterine volume flow remained at ~40-75% of resting values (Salvesen *et al.*, 2012). However, during a bout of vigorous exercise that elicited a maximum maternal heart rate above 90%, fetal bradycardia was induced. Additionally, during exercise at >90% maternal heart rate, the mean uterine artery volume blood flow was reduced to ~25-60% of resting values (Salvesen *et al.*, 2012). The human fetus normally has a higher temperature than its mother and the principal route of fetal heat dissipation (Macaulay *et al.*, 1992) is through uterine-placental circulation. Any impedance in maternal systemic and peripheral heat loss may affect fetal health.

Peripheral dry heat loss responses in skin blood flow, skin temperature and peripheral vascular resistance (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Jones *et al.*, 1985; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Hartgill *et al.*, 2011; Iacobaeus *et al.*, 2017), parallel the systemic responses (i.e., cardiac output, stroke volume, blood volume and vascular resistance) (Pivarnik *et al.*, 1990; Vähä-Eskeli *et al.*, 1991b; Clapp & Capeless, 1997). In resting conditions, skin blood flow and skin temperature progressively increased and peripheral vascular resistance decreased from early to late pregnancy (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Jones *et al.*, 1985; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Hartgill *et al.*, 2011; Iacobaeus *et al.*, 2017). A study that measured skin temperature using thermistors (in 4 locations) from rest to exercise across the stages of pregnancy (Jones *et al.*, 1985). Consistently, from rest to the end of exercise, skin temperature remained higher in late pregnancy compared to early pregnancy (Jones *et al.*, 1985). In contrast, a study using digital thermal imaging compared skin temperatures at various body regions (i.e., chest, stomach, and upper/lower back) reported that pregnant and non-pregnant women had similar changes in skin temperature in response to exercise from resting/baseline (Simoes *et al.*, 2012). Likewise, another study found similar change in skin temperature during rest to exercise between pregnant and non-pregnant controls (Vähä-Eskeli *et al.*, 1991a). Nevertheless, post-exercise recovery responses in skin temperature decreased at a faster rate in the pregnant compared to the non-pregnant group decreased at a faster rate (Vähä-Eskeli *et al.*, 1991a). Several studies compared women with a healthy pregnancy to those with hypertension, to evaluate the impact of high maternal blood pressure on vasculature function (Tur *et al.*, 1992a; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Cankar *et al.*, 2010). The predominant outcome in cutaneous microvasculature demonstrated that women with hypertension during pregnancy had greater vasoconstrictive responses and reduced skin blood flow compared to women experiencing a healthy pregnancy (Tur *et al.*, 1992a; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Cankar *et al.*, 2010).

3.3 Summary of behavioural and cultural related heat loss responses in pregnancy

Pregnancy is a unique phase in life; cultural beliefs and attitudes may influence thermal behavioural responses (e.g., staying indoors during peak midday high temperatures or taking more rest/breaks throughout the day) (Ejidokun, 2000; Downey, 2008; Basu *et al.*, 2010; Wulandari &

Klinken Whelan, 2011). In a study that used qualitative in-depth interviews regarding beliefs, attitudes, and behaviours during pregnancy in pregnant women from Bali, Indonesia.(Wulandari & Klinken Whelan, 2011). In essence, the women believed that to maintain a healthy infant, they need to take good care of themselves, follow traditional rituals (i.e., herbal remedies), meditate, and pray to God. Religious beliefs also encouraged women to pray/meditate more, which is generally an indoor behaviour allowing them to take more rest/breaks throughout the day and avoid sun/humidity/high temperature outside. Responses from several participants indicated that family members played a crucial role in influencing their behaviors by encouraging rest and proper diet habits. The influence of community on thermoregulatory related behaviours of pregnant women was also documented using qualitative methods including focus-group discussions, observational data gathered on site visits and in-depth interviews in Lagos, South-Western Nigeria (Ejidokun, 2000). The authors (Ejidokun, 2000) reported that pregnancy was not viewed as a functional impairment or illness, if otherwise healthy, women were encouraged to continue their regular daily activities. For example, household maintenance/cooking, caring for other children and/or other work. There was one crucial expectation: due to a higher risk of heat related injuries for mother and fetus, pregnant women were expected to remain indoors resting during what was considered midday (Ejidokun, 2000).

Maintaining a vigorous exercise regimen throughout pregnancy was not recommended by the support group of highly trained pregnant women (Downey, 2008) interviewed women who continued a high intensity exercise routine during their pregnancy, and described their experiences (Downey, 2008). The women who continued vigorous exercise throughout pregnancy believed it was part of maintaining a healthy pregnancy and supporting their fetus (Downey, 2008). Despite cultural and family pressure to stop, the women overcame the pressure/conflict by seeking a supportive network that encouraged vigorous exercise during pregnancy (Downey, 2008). Categorically, parameters including socio-economic status, age and ethnicity may be predictors of hazardous behaviours in pregnant women. From an epidemiological perspective that conducted a population-based study of ambient temperature and pre-term delivery in the state of California, United States of America (Basu *et al.*, 2010). They reported that maternal race/ethnicity (i.e., African and Asian American) and maternal age (i.e., ~20 y and under) served as effective markers of socio-economic status and demonstrated that women of African and Asian American race/ethnicity and ~ 20 years of age partook in more risky behaviour (e.g., poor diet practices, alcohol consumption, smoking, poor environmental exposures) especially during the hot summer seasons compared to other maternal groups (Basu *et al.*, 2010).

PRISMA 2009 Flow Diagram

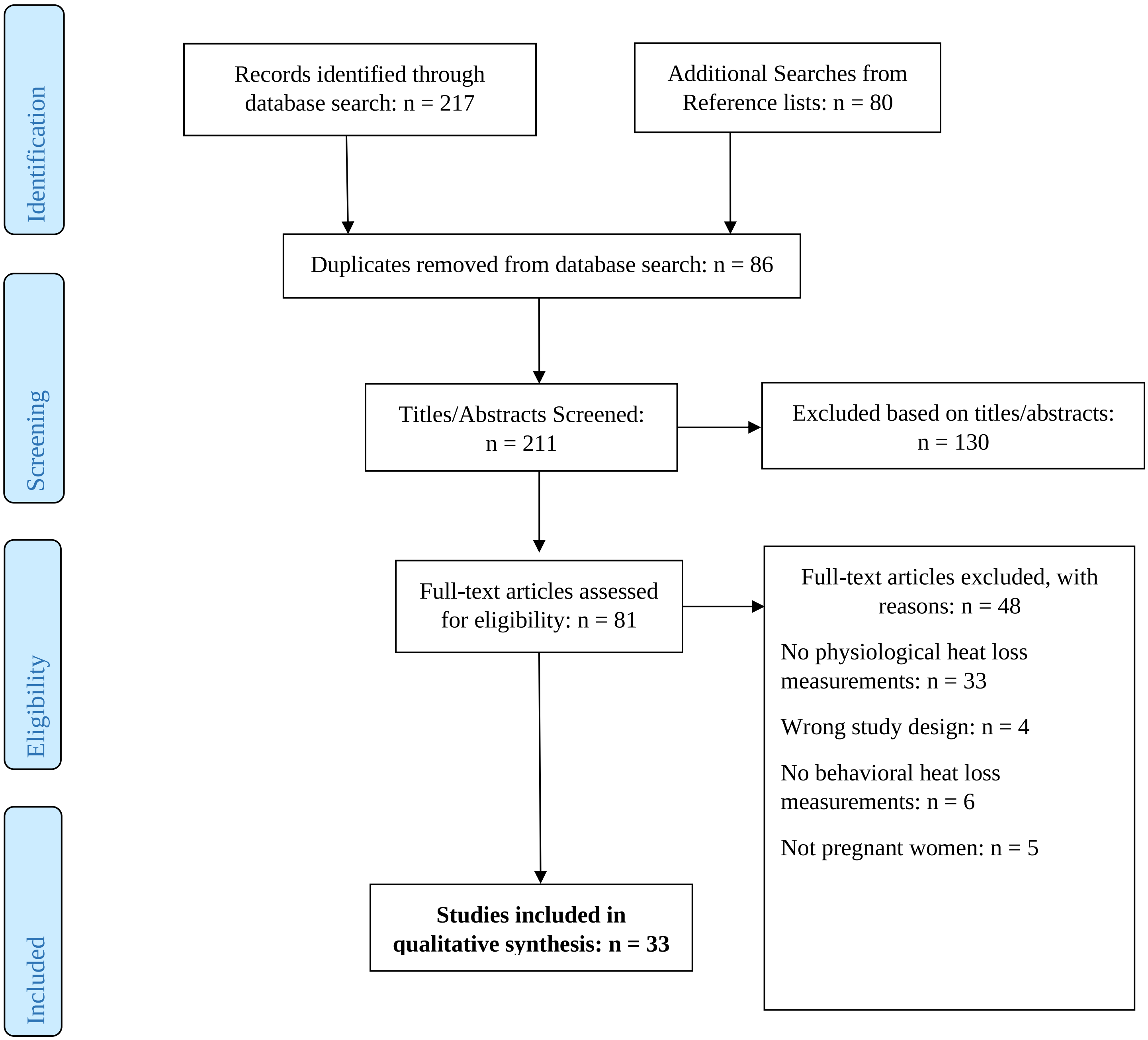

Figure 1 PRISMA flow diagram for study selection

Table 3. Study characteristics, including heat loss measurements and relevant main findings to this current scoping review.

Author (year)	Country	Total sample size	Description of methods	Heat loss measurements	Main findings related to the review questions
(Anim-Nyame *et al.*, 2000)	United Kingdom	59	Longitudinal quantitative study in healthy and hypertensive pregnant women. They used venous occlusion plethysmography at rest.	Calf blood flow (mL/100mL)	1. Blood flow increased with gestation in normal pregnancy. 2. Chronic hypertension reduced blood flow responses.
(Baciuk *et al.*, 2008)	Brazil	71	Randomized control quantitative study across pregnancy. Participants either partook in regular aquatic exercise or no physical activity throughout pregnancy.	Skin temperature (°C) and cardiac output (L/min)	1. Skin temperature in exercise group was higher throughout exercise protocol. 2. Cardiac output increased across pregnancy and was higher at the end of exercise in the exercise group.
(Basu *et al.*, 2010)	United States of America	58,681	Case-crossover analysis across pregnancy. A population based epidemiologic study of ambient temperature and preterm delivery.	Skin temperature (°C), race, ethnicity, and maternal age associated with thermal behavioural responses.	1. A significant positive association between apparent temperature and preterm delivery during warm season. 2. Maternal race/ethnicity and maternal age served as an effective marker of socio-economic status and unsafe behavioural patterns compared to other maternal groups.
(Beinder *et al.*, 1990)	Switzerland	19	Quantitative experimental analysis in pregnant and non-pregnant women. Skin temperature measured at rest and after cold stimulus/venous occlusion.	Forearm and hand skin temperature (°C).	1.No skin temperature differences between non-pregnant and pregnant groups. 2. In the pregnant group skin temperature was higher in the hand compared to forearm. 3. Skin temperature decrease was reduced in the pregnant group after cold stimulus and venous occlusion.

(Cankar *et al.*, 2010)	Slovenia	38	Quantitative experimental analysis in non-pregnant women, healthy and gestational hypertensive pregnant women. Laser Doppler flux of skin blood flow was measured at rest prior and post a local cooling (15°) protocol on the left hand.	Skin blood flow (perfusion units- using laser Doppler flowmetry) on the left hand.	1. Cutaneous microvasculature response to local cooling is lower in women with gestational hypertension compared to the other groups. 2. A greater vasoconstrictive response was measured in the gestational hypertensive group.
(Chapman *et al.*, 1998)	United States of America	11	A longitudinal quantitative study to examine systemic and renal hemodynamics (using modified cardiac output rebreathing technique) throughout pregnancy compared to non-pregnant controls. Measurements were done after 1 hour in the left lateral decubitus position.	Total blood volume (mL/kg), cardiac output (L/min), and peripheral vasodilation.	1.Peripheral vasodilation occurs early in pregnancy, prior to full placentation. 2. As pregnancy progresses vasodilation increases and results in mean arterial pressure associated with a rise in cardiac output.
(Clapp, 1991)	United States of America	18	A longitudinal quantitative study in women who started non-pregnant then returned throughout pregnancy. At rest, exercise and recovery, weight change, metabolic rate and rectal temperature were taken.	Onset of sweating determined by individual's subjective sensation of sweating at a given rectal temperature (°C) and weight change (kg).	1.Onset of sweating occurred at a lower rectal temperature as pregnancy progressed. 2. Increase in weight change as pregnancy progressed pre-to post- exercise.
(Clapp & Capeless, 1997)	United States of America	30	A longitudinal study in physically active women who started non-pregnant then returned throughout pregnancy. Cardiovascular measurements taken during rest in left lateral decubitus position.	Cardiac output (L/min), stroke volume (mL), vascular resistance (dynes/cm/sec^5)	1.Parous women exhibited greater cardiac output, stroke volume and reduced peripheral vascular resistance compared to nulliparous.

(Clapp *et al.*, 2000)	United States of America	12	Prospective randomized control study of physically active and non-active women across pregnancy. Blood flow and volume was measured during rest in left lateral decubitus position, standing rest and during weight bearing exercise.	Blood flow (mL/min) and portal vein diameter (mm) measured using ultrasound.	1.60% increase in splanchnic blood flow early in pregnancy and peaked end of second trimester. 2. Physically active pregnant women peaked splanchnic blood flow earlier than non-active pregnant women. 3. From standing rest to exercise portal vein blood flow decreased, but in physically active pregnant women decrease was blunted compared to non-active controls.
(Downey, 2008)	Canada	10	A qualitative grounded theory thesis study in pregnant women who engaged in a highly active lifestyle throughout their pregnancy. A semi-structured, open-ended interview exploring a) women's lifestyle behaviours in general, b) workout regiment, c) information received by health care professional.	Interview responses of pregnant women indicating maintaining exercise intensity throughout pregnancy.	1.Women continued vigorous exercise throughout pregnancy. 2. They believed it provided a healthy pregnancy for mother and baby. 3. They experienced lots of pressure to stop due to beliefs the intensities would harm the baby. 4. They overcame the conflict by seeking supportive networks.
(Dunlap, 2003)	United States of America	12	A randomized control thesis study in healthy pregnant women. Metabolic rate, heart rate, and total body water losses were measured pre- and post-resting baseline, structured aquatic exercise class for and recovery in either a 27.7°C or 33.5°C pool.	Total body sweat loss (kg), pre- and post-exercise protocol.	1.Total sweat loss was significantly higher in the treatment (33.5°C) versus control (27.7°C) pool.

(Ejidokun, 2000)	Nigeria	23	Qualitative descriptive study, interviewing pregnant women in Nigeria.	The interviews included focus-group discussions, observational data gathered on site visits and in-depth interviews.	1. Pregnant women are encouraged to continue their daily activity and work because pregnancy is not considered an illness. 2. Culturally it is not acceptable for pregnant women to go outside midday due to safety reasons.
(Erkkola *et al.*, 1992)	Finland	8	A quantitative experimental study in healthy pregnant women. Participants partook in an exercise test on a cycle ergometer after a resting baseline period.	Systolic/Diastolic ratio in the uterine artery measured using a colour Doppler system.	1.Uterine artery blood flow decreased with increased exercise intensity. 2. No change across pregnancy during exercise in umbilical artery flow velocity.
(Fawer *et al.*, 1978)	Switzerland	118	A quantitative experimental study in non-pregnant controls on contraceptives and pregnant women across pregnancy. Blood flow and venous capacitance was determined by venous occlusion plethysmography in basal conditions, in the recumbent position.	Forearm blood flow (mL/min/100 mL tissue) was measured with a water-filled plethysmograph.	1.Forearm blood flow and venous distensibility was greater in the pregnant women compared to the non-pregnant controls. 2. The same values increased across pregnancy (from first to third trimester).
(Hartgill *et al.*, 2011)	Norway	15	A longitudinal study in healthy pregnant women throughout pregnancy. Tympanic temperature and laser Doppler ultrasound measurements during rest in different ambient temperatures.	Velocity waveforms measured with Doppler ultrasound to measure atrio-venous anastomosis and blood flow.	1.Arteriovenous anastomosis by third trimester were more dilated than earlier in pregnancy. To reach a thermoneutral zone occurred 4°C lower, increasing heat loss.

(Iacobaeus *et al.*, 2017)	Sweden	60	A longitudinal study in healthy pregnant women compared to post-partum. Microvasculature dilation was measured using laser Doppler perfusion imaging and iontrophetic administration of acetylcholine (Ach) and single-nucleotide polymorphism (SNP). Skin microvasculature was measured pre-, during and post- administration of ACh and SNP.	Skin microvasculature dilation (mm)/flux (m/s) measured using laser Doppler perfusion imaging and ACh and SNP infusion	1.Continual increase in diameter of conduit arteries and microvascular vasodilator reactivity as pregnancy progressed. 2. Forearm skeletal muscle vasculature, microvasculature reactivity to ACh increased in pregnancy – which suggest greater endothelium dependent microvascular function.
(Jeffreys *et al.*, 2006)	United States of America	14	A quantitative experimental study in physically active pregnant women after 28 weeks of gestation. Uterine blood flow was measured during rest and exercise in the left-lateral decubitus position in both groups.	Volume flow (cc/minute) of the uterine artery was measured using and ultrasonography.	1.Uterine blood flow decreased during supine rest due to vasoconstriction due to reduced venous return and cardiac output. 2. Supine exercise increased venous return, cardiac output, and blood pressure, increasing uterine blood flow more than supine rest.
(Jones *et al.*, 1985)	United States of America	4	A longitudinal study throughout healthy pregnancy and postpartum. A weight bearing exercise protocol used to measure skin temperature, sweat losses from weight change and percent plasma change.	Skin temperature thermistors (°C) placed on the chest, arm, back and thigh. Change in body weight pre- and post-exercise (kg). Relative plasma volume loss (%).	1.Skin temperature at rest was highest in the third trimester. 2. In exercise skin temperature remained highest in the third trimester. 3. In recovery, skin temperature in third trimester and postpartum remained higher than earlier in pregnancy.

(Macaulay *et al.*, 1992)	United Kingdom	36	A quantitative experimental study in pregnant women near term. Temperature sensors were placed between the fetal scalp and maternal uterine wall above the cervix, throughout labour.	Temperature sensors (°C).	1.Fetal temperature change is related primarily to maternal temperature. 2. Fetal heart rate changes correlate better with maternal temperature. Due to 85% of fetal heat is transferred by the placental circulation. 3. A rise in maternal temperature would diminish heat transfer across the placenta and warmer blood perfuse the fetal circulation.
(McMurray *et al.*, 1993)	United States of America	7	A cross-over randomized control study in healthy pregnant women (25 to 26 weeks gestation). Participants completed a submaximal cycle ergometer test. Following a resting period, exercise trial on land or in water (30°C).	Skin temperature (°C) thermistors placed on forehead, chest, back, upper-arm, and thigh. Estimated evaporative heat loss based on weight change (kg).	1.Skin temperature was lower in the water trial. 2. Heat storage and heat loss was greater in the land trial.
(Moore *et al.*, 1988)	United States of America	11	A quantitative experimental study in healthy pregnant women from 16 to 28 weeks gestation. After resting baseline, participants cycled, and uterine artery blood flow was measured pre- and post-exercise.	Uterine artery velocity waveforms were scanned using a Doppler transducer.	1.The mean difference in pre- and post-exercise was similar in uterine blood flow.
(Myhrman *et al.*, 1980)	Sweden	14	A longitudinal study in healthy pregnant women and postpartum. During resting measurements of blood pressure, hand blood flow and peripheral vascular resistance was calculated.	Hand blood flow (mL/min/100 mL) and peripheral vascular resistance (PRU) using occlusion plethysmography.	1.Hand blood flow increased progressively from early to term pregnancy. 2. Peripheral vascular resistance decreased from early to term pregnancy.

(Ohlmann *et al.*, 2001)	Germany	95	A longitudinal study in healthy and hypertensive pregnant women throughout pregnancy and postpartum. A video capillary microscopy and erythrocyte velocity in the venules measured under resting conditions and reactive hyperaemia.	Periungual capillary microscopy used to measure peripheral microcirculation (mm/s). Erythrocyte velocity (mm/s) in the venules using bright-field microscope connected to a video chain.	1.Increase in erythrocyte velocity from early to late pregnancy. 2. There is an increase in peripheral vasodilation from early to late pregnancy.
(Pivarnik *et al.*, 1990)	United States of America	7	A longitudinal study in healthy pregnant women from late pregnancy to postpartum. Metabolic and cardiovascular responses to stationary cycling and treadmill walking via Fick technique.	Cardiac stroke volume was calculated by dividing heart rate and cardiac output as determined by Fick's equation: CO = VO2/a-vO2 difference.	1.Cycling and treadmill walking resulted in increased metabolic rate, cardiac output at 37 weeks gestation compared to postpartum. 2. Stroke volume were also greater at 37 weeks gestation compared to postpartum.
(Salvesen *et al.*, 2012)	Norway	6	A quantitative experimental study in pregnant elite athletes. Participants ran several submaximal tests. The maternal-fetal circulation was measured with Doppler ultrasound of the uterine and umbilical arteries at rest, during and after exercise.	Proportional change in uteroplacental blood flow (%) measured with Doppler ultrasound pre-, during and post- exercise using a Logic 7 Device with a multi-frequent curvilinear transducer.	1.Uterine artery blood flow reduced ~70% after warm-up and stayed at ~58% of initial exercise. 2. Fetal heart rate was within normal range during exercise < 90% maximal heart rate. 3. Above 90% maximal heart rate high umbilical/ uterine artery was below 50% resting value.
(Sillero-Quintana *et al.*, 2012)	Spain	28	A quantitative experimental study in healthy pregnant women. Participants were set up with infrared thermography and partook in low intensity yoga or aquatic activity.	Thermograms were recorded with an infrared camera. Skin temperature (°C) measured at regions of interest, including upper/lower limbs, trunk, belly, and breast.	1.In yoga, the area with a higher skin temperature increase after exercise is the belly (0.77°C), followed by breast (0.52°C) and both significantly higher than other regions of interest.

(Simoes *et al.*, 2012)	Portugal	41	A quantitative experimental study in healthy pregnant and non-pregnant women. An infrared camera was used to capture rest standing thermal images of regions of interest, breast, upper/lower abdomen, upper back and lumbar.	The FLIR SC640 infrared camera was used to capture thermal images in regions of interest while standing.	1.Thermal symmetry between posterior and anterior were similar in pregnant group. 2. The regions of interest were comparable between pregnant and non-pregnant controls.
(Stark *et al.*, 2006)	Australia	102	A quantitative experimental study in healthy and preeclamptic pregnant women. Microvascular reactivity in normal and preeclamptic women and determine if fetal sex impacts maternal microvascular function.	Skin blood flow (PU) measured using Periflux 5001 laser Doppler temperature regulated iontophoresis probe (corticotropin-releasing hormone) and temperature regulated probe for skin blood flow.	1.Decrease in skin blood flow in preeclamptic women with male fetus. 2. Female fetus did not change basal skin blood flow between healthy and preeclamptic women.
(Szymanski & Kogutt, 2018)	United States of America	45	A prospective cross-sectional study in healthy pregnant women in two groups: 1) exercisers 2) non-exercisers. Uterine artery functionality after individually prescribed exercise, 1) moderate-intensity exercise in both non-exercisers and exercisers and 2) vigorous-intensity exercise in exercisers	Ultrasound scanning measured uterine artery flow. Doppler was used with a Phillips IU22 ultrasonography system.	1.During moderate-intensity session, mean uterine artery Doppler indices did not change for either group.

(Tur *et al.*, 1992a)	Israel	33	A quantitative experimental study in non-pregnant, healthy, and hypertensive pregnant women late in pregnancy. Responses to four vasoactive stimuli were studied: isometric and cognitive activities, cutaneous post ischemic reactive hyperemia and local heating. The first two are vasoconstrictive and the latter two were vasodilative.	A laser Doppler flowmeter was used to assess skin blood flow (PU) changes.	1. Isometric test: healthy pregnant group had the lowest decrease in blood flow compared to other groups. 2. Cognitive test: both pregnancy groups had similar responses, and both had lower blood flow compared to non-pregnant group. 3. Reactive hyperemia: baseline blood flow same across all groups. 4. Thermal test: Similar across 3 groups.
(Vähä-Eskeli *et al.*, 1991a)	Finland	61	A quantitative experimental study in healthy pregnant and non-pregnant controls. This study investigated effects of short-term heat stress in early and late pregnancy. Rectal and skin temperatures were measured during resting period followed by thermal stress and a recovery period.	Skin temperature (°C) using an electric thermometer place on the right shoulder.	1. Similar skin temperature across all groups. 2. Late pregnancy group skin temperature reached steady state earlier in heat stress compared to other groups. 3. Decline in skin temperature during recovery was faster and more profound in the late pregnancy group compared to other groups.
(Vähä-Eskeli *et al.*, 1991b)	Finland	47	A quantitative experimental study in healthy pregnant and non--pregnant women. The aim was to measure circulatory reactions to thermal stress and recovery.	Stroke volume measured with impedance cardiograph. Cardiac output = stroke volume multiplied by heart rate. Peripheral vascular resistance = mean arterial pressure divided by cardiac output.	1.Prior to heat stress stroke volume was greatest in late pregnancy group. End of heat stress, stroke volume was similar in all groups. 2. Cardiac output was similar across all groups. 3. Peripheral vascular resistance in late pregnancy had small reduction during thermal stress compared to other groups.

(Wulandari & Klinken Whelan, 2011)	Indonesia	18	A qualitative mixed methods study in healthy pregnant women. This study describes the findings of qualitative interviews with Indonesian pregnant women to explore their beliefs, attitudes, and behaviours regarding pregnancy.	An interview guide was developed for participants to use their own words. The interview guide was designed with questions regarding information on health benefits, attitudes and practices during pregnancy and ideas and practices about managing a healthy pregnancy.	1. Regular rest was of valuable importance to ensure healthy pregnancy. 2. Religious practice including prayer and meditation.

4.0 Discussion

The main objective of this scoping review was to identify studies that measured heat loss responses in pregnant women, based on behavioural responses (i.e., sociodemographic factors, culture/religion and/or personal preferences) or physiological responses, including evaporative heat loss (i.e., sweating or weight change) and/or dry heat loss (i.e., blood flow/skin temperature) during exercise or passive heat exposure. Collectively, the findings indicated that sociodemographic factors, cultural/religious beliefs, and personal preferences all play a crucial role in behavioural responses in pregnant women. Furthermore, as illustrated in Figure 2 the physiological responses in evaporative and dry heat loss revealed that the greatest blood flow (i.e., greater dry heat loss) (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Jones *et al.*, 1985; Moore *et al.*, 1988; Beinder *et al.*, 1990; Pivarnik *et al.*, 1990; Vähä-Eskeli *et al.*, 1991a; Vähä-Eskeli *et al.*, 1991b; Erkkola *et al.*, 1992; Macaulay *et al.*, 1992; Tur *et al.*, 1992b; McMurray *et al.*, 1993; Clapp & Capeless, 1997; Chapman *et al.*, 1998; Anim-Nyame *et al.*, 2000; Clapp *et al.*, 2000; Ohlmann *et al.*, 2001; Jeffreys *et al.*, 2006; Stark *et al.*, 2006; Baciuk *et al.*, 2008; Cankar *et al.*, 2010; Hartgill *et al.*, 2011; Salvesen *et al.*, 2012; Sillero-Quintana *et al.*, 2012; Simoes *et al.*, 2012; Iacobaeus *et al.*, 2017; Szymanski & Kogutt, 2018) and sweat losses (i.e., evaporation) (Jones *et al.*, 1985; Clapp, 1991; McMurray *et al.*, 1993; Dunlap, 2003) at rest and during exercise occurred in late pregnancy compared to both early pregnancy and non-pregnant women (Jones *et al.*, 1985; Moore *et al.*, 1988; Pivarnik *et al.*, 1990; Clapp, 1991; Vähä-Eskeli *et al.*, 1991b; Erkkola *et al.*, 1992; Macaulay *et al.*, 1992; McMurray *et al.*, 1993; Clapp & Capeless, 1997; Chapman *et al.*, 1998; Clapp *et al.*, 2000; Dunlap, 2003; Jeffreys *et al.*, 2006; Baciuk *et al.*, 2008; Salvesen *et al.*, 2012; Simoes *et al.*, 2012). The teratogenic risks associated with hyperthermia in pregnancy, has promoted an appreciable amount of research into understanding core temperature responses in various environments and intensities of exercise, however, in most cases heat loss mechanisms were not collectively measured (Jones *et al.*, 1985; McMurray & Katz, 1990; Tuffnell *et al.*, 1990; Clapp, 1991; Vähä-Eskeli *et al.*, 1991a; McMurray *et al.*, 1993; O'Neill, 1996; Lindqvist *et al.*, 2003; Brearley *et al.*, 2015; Petrov Fieril *et al.*, 2016b). It is known that to maintain a stable core temperature during heat stress, heat loss mechanisms must enable heat transfer either through evaporation of sweat and/or dry heat loss (i.e., blood flow and skin temperature). Our scoping review has shown there to be a scarcity of research assessing the heat loss mechanisms in pregnant women.

Each of the studies that assessed evaporative heat loss from sweating in pregnancy utilized a different exercise protocols/intensity (Jones *et al.*, 1985; Clapp, 1991; McMurray *et al.*, 1993; Dunlap, 2003) making direct comparisons problematic. Nevertheless, the predominant outcome reported was a greater sweat loss in late compared to early and pre-pregnancy (Jones *et al.*, 1985; Clapp, 1991; McMurray *et al.*, 1993; Dunlap, 2003), although gestational weight gain was not accounted for in the measurements. Considering pregnant women consistently gain weight compared to non-pregnant controls, the increase in weight generally results in higher oxygen consumption (VO_2 in L/min) during exercise (Cramer & Jay, 2016). A given weight-bearing task and the rate of metabolic heat production is determined by oxygen consumption (VO_2 in L/min), for the same exercise intensity, a greater weight typically results in elevated oxygen consumption (Cramer & Jay, 2016). For example, a study reported a decrease in maximum rectal temperature by 0.3°C from pre to late pregnancy during an exercise intensity fixed at ~64% VO_{2peak} (Clapp, 1991). The increasing gestational weight gain from pre-pregnancy at 61.5 ± 2 kg to late pregnancy at 79.2 ± 3.2 kg, reduced the intensity required to attain the same oxygen consumption (~64% VO_{2peak}) (Clapp, 1991). Correspondingly, the same authors (Clapp, 1991) reported an increase in total body sweat losses, thermo-sensitivity and decrease in onset threshold (i.e., rectal temperature associated to increase in sweating) in late compared to early pregnancy/non-pregnant women. In other words, a lower onset rectal temperature for sweating, and a greater rate at which sweating increases in response to the changes in core temperature. The rise in thermo-effector response of sweating from early/pre- to late pregnancy during fixed weight bearing exercise may be due to the large differences in body weight across pregnancy, compared to non-pregnant women (Hammel, 1968; Gagge & Gonzales, 1996). Unfortunately, the measurement of onset threshold was based on the participant's perception of sweating by indicating at which point they 'felt' they started to sweat, reducing the reliability of the measurement by relying on the participant's subjective sense of sweating onset (Clapp, 1991). Commonly used equipment to measure sweating onset/rate precisely and objectively is a ventilated sweat capsule. Employing ventilated sweat capsules, enables sweat rate to be calculated as the product of absolute humidity and flow rate expressed relative to the surface area covered by the capsules, averaged every minute (expressed in $mg \cdot cm^{-2} \cdot min^{-1}$).The outcomes related to sweating in this scoping review suggest there may be an opportunity to bridge the gap between understanding the influence of gestational weight gain on heat production during exercise and using an objective measurement of sweat rate such as ventilated sweat capsules to measure thermo-sensitivity.

Dry heat loss mechanisms are typically measured in skin temperature and skin blood flow responses. In response to a high metabolic heat load, a research study reported highest skin temperature in late compared to early pregnancy in aerobically fit pregnant participants (Jones *et al.*, 1985). The participants ran for 30 min at 80-90% maternal maximal heart rate and end-exercise core temperature reached 38.3°C (Jones *et al.*, 1985). Accordingly, a separate study continued to measure skin temperature following exercise, the authors reported enhanced dry heat loss function in late pregnancy compared to non-pregnant women as skin temperature decreased at a faster during post-exercise recovery (Vähä-Eskeli *et al.*, 1991a). Contrarily, this scoping review revealed some disparate findings in skin temperature responses, where no differences in skin temperature were reported between pregnant (from early to late pregnancy) and post-partum or non-pregnant women (Beinder *et al.*, 1990; Vähä-Eskeli *et al.*, 1991a; McMurray *et al.*, 1993). Although in these cases, the design of the studies or equipment may be a source of discrepancy in results, in two of the studies (Beinder *et al.*, 1990; McMurray *et al.*, 1993) cold temperature contact or water immersion was used and may have blunted changes in skin temperature (Beinder *et al.*, 1990; Vähä-Eskeli *et al.*, 1991a; McMurray *et al.*, 1993). In addition to the disparate findings, equipment used may have diminished the sensitivity to detect differences between groups. For example, skin temperature was measured at one location (shoulder) using an electric thermometer, which may have not been as sensitive as a thermistor (for example) to detect changes in skin temperature between the groups, and rather only robust changes in skin temperature were reported (Vähä-Eskeli *et al.*, 1991a).

Peripheral skin blood flow is another relevant measurement of dry heat loss. Studies included in this review were limited to measuring peripheral skin blood flow during resting conditions, and these responses could not be extended to exercise (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Tur *et al.*, 1992a; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Cankar *et al.*, 2010). The principal outcome, regardless of assessment methodology (laser Doppler, plethysmography, ultrasound, laser Doppler perfusion imaging, iontophoretic administration of vasodilators and capillary microscopy), is that peripheral skin blood flow gradually increased and peripheral vascular resistance progressively decreased from early to late pregnancy (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Tur *et al.*, 1992a; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Cankar *et al.*, 2010; Hartgill *et al.*, 2011). Furthermore, any comparisons made with non-pregnant or hypertensive women, demonstrated that there was a greater increase in skin blood flow and decrease in peripheral vascular resistance in healthy pregnancy (Fawer *et al.*, 1978; Myhrman *et al.*, 1980; Tur *et al.*, 1992a; Anim-Nyame *et al.*, 2000; Ohlmann *et al.*, 2001; Cankar *et al.*, 2010; Hartgill *et al.*, 2011; Iacobaeus *et al.*, 2017). Meaning the cardiovascular-related impairments in hypertension during pregnancy become a barrier in heat loss and overall thermoregulatory function. Dry heat loss mechanisms, including peripheral microvasculature and skin temperatures have been shown to be closely related to the perceptual responses found in both thermal sensation and thermal comfort (Gagge *et al.*, 1969; Marks & Gonzalez, 1974; Wang *et al.*, 2007; Zhang *et al.*, 2010). Thermal sensation provides information regarding the individual's conscious feeling of being warm or cold (Nakamura *et al.*, 2008). Whereas, thermal comfort is more of a state of mind that conveys satisfaction within a given environment (Nakamura *et al.*, 2008). Both Thermal sensation and comfort scales link physiological dry heat loss responses to perceptual/subjective measurement of heat load. Therefore, both scales would provide a practical assessment tool that would be helpful to understand maternal-fetal protective responses of pregnant women across various heat loads and during exercise.

Systemic vascular responses including, cardiac output, stroke volume, vascular resistance, uterine, umbilical, and utero-placental blood flow are indirect mechanisms that contribute to dry heat loss. Fortunately, the studies examined in this scoping review included both rest and exercise protocols (Moore *et al.*, 1988; Pivarnik *et al.*, 1990; Erkkola *et al.*, 1992; Clapp *et al.*, 2000; Jeffreys *et al.*, 2006; Baciuk *et al.*, 2008; Salvesen *et al.*, 2012; Szymanski & Kogutt, 2018). At rest, a rise in stroke volume (i.e., difference in preload and after load of blood pumped into the aorta) results from a surge of blood volume in pregnancy, precipitating an increase in cardiac output since it is the product of stroke volume and heart rate (Vähä-Eskeli *et al.*, 1991b; Clapp &

Capeless, 1997; Chapman *et al.*, 1998; Clapp *et al.*, 2000; Tan & Tan, 2013). Also, during pregnancy, splanchnic blood flow to the uterus and placenta constitutes approximately 25% of cardiac output and is important for fetal development (Thornburg *et al.*, 2000; Tan & Tan, 2013). Predominantly, during exercise cardiac output, blood flow/volume and stroke volume increased, and vascular resistance decreased from early to late pregnancy (Pivarnik *et al.*, 1990; Clapp *et al.*, 2000; Baciuk *et al.*, 2008). Given the influx of blood volume as pregnancy progresses, it was demonstrated that the redistribution of blood flow during exercise to skin and working muscle does not impair fetal health if intensity does not exceed 90% maximal maternal heart rate (Salvesen *et al.*, 2012). The systemic response from rest to exercise would ideally extend to peripheral skin blood flow, considering a study reported a persistent improvement in endothelial function due to increased vascular nitric oxide availability during pregnancy (Iacobaeus *et al.*, 2017). Therefore, an improved endothelial-dependant vasodilation throughout pregnancy. Despite the pertinent evidence of the influence of pregnancy on skin microvasculature function, current literature does not include measurements of skin blood flow in pregnant women during exercise. In addition to the active physiological system of thermoregulation, there is an important behavioural response. The perception of change in environment may produce a behavioural response, such as a change in posture, seeking shade in the summer months, clothing choices or amount of movement/rest within a given environment. The interrelating factors influencing behavioural thermal responses during pregnancy are unique considering the time is transient (i.e., nine months for humans) and comes with a responsibility of another life. Certain determinants of behavioural heat loss systems during pregnancy include, personal preferences/priorities (Downey, 2008), cultural values, religion (Ejidokun, 2000; Wulandari & Klinken Whelan, 2011) and physical or social environments (Basu *et al.*, 2010). They can also be modified by sociodemographic factors such as ethnicity, age, socioeconomic status, education, and income (Basu *et al.*, 2010). In circumstances in which pregnant women embraced cultural/religious values, they were encouraged to continue their daily activities/work yet pray/meditate more frequently (Wulandari & Klinken Whelan, 2011) and avoid outdoors during the midday when the temperature is the highest (Ejidokun, 2000). These behaviours indirectly provide more rest indoors in cooler environments. On the other hand, pregnant women who prioritized maintaining their high level of fitness by continuing to engage in high intensity training similarly to pre-pregnancy, above their cultural expectations were faced with stigma from their community (i.e., family members, friends, and coworkers) (Downey, 2008).The findings highlight the need to provide culturally tailored interventions and health messaging that would dispel the misconception that regular physical activity will increase the risk of heat related injuries more in pregnant women compared to non-pregnant women.

This review is the first to summarize the literature related to heat loss responses in pregnant women. We followed the Arksey and O'Malley framework (Arksey & O'Malley, 2005), and Peters *et al.* PRISMA-ScR checklist (Peters *et al.*, 2020), to fulfill a comprehensive and systematic search synthesis, including two independent reviewers for screening and data extraction. Scoping reviews are criticized for their lack of quality assessment, and our results were only synthesized narratively, which could be considered a limitation. Considering the scarce availability of research on this topic, a systematic review and meta-analysis would presently not be an effective method for analyzing the literature. In this case, our scoping review effectively provides an overview of what is currently known about heat loss in pregnant women and has identified research gaps thereby informing future areas of investigation.

5.0 Conclusion

The results of our scoping review, illustrated in Table 4, provide important key findings regarding physiological heat loss measurements in pregnancy, including cardiac output, stroke volume, skin blood flow, vascular resistance, skin temperature and sweating. Also, the importance of the following parameters when considering future research directions to provide a more comprehensive understanding of heat loss mechanisms in pregnant women: 1) total body mass of participants must be accounted for during exercise, where comparisons between groups are made with similar weights, 2) in addition to total body sweat losses, using ventilated sweat capsules will provide a more accurate measurement of sweat rate across pregnancy, 3) thermal sensation/comfort scales during heat stress will provide a link between physiological and perceptual responses in pregnant women, and 4) providing culturally tailored recommendations for physical activity, will encourage pregnant women to remain active during pregnancy, without concern or conflict from their community. Furthermore, complimenting physiological responses with subjective perceptual responses such as thermal sensation/comfort scale could potentially be used as an added tool in the current exercise guidelines to avoid overexertion in pregnant women during exercise.

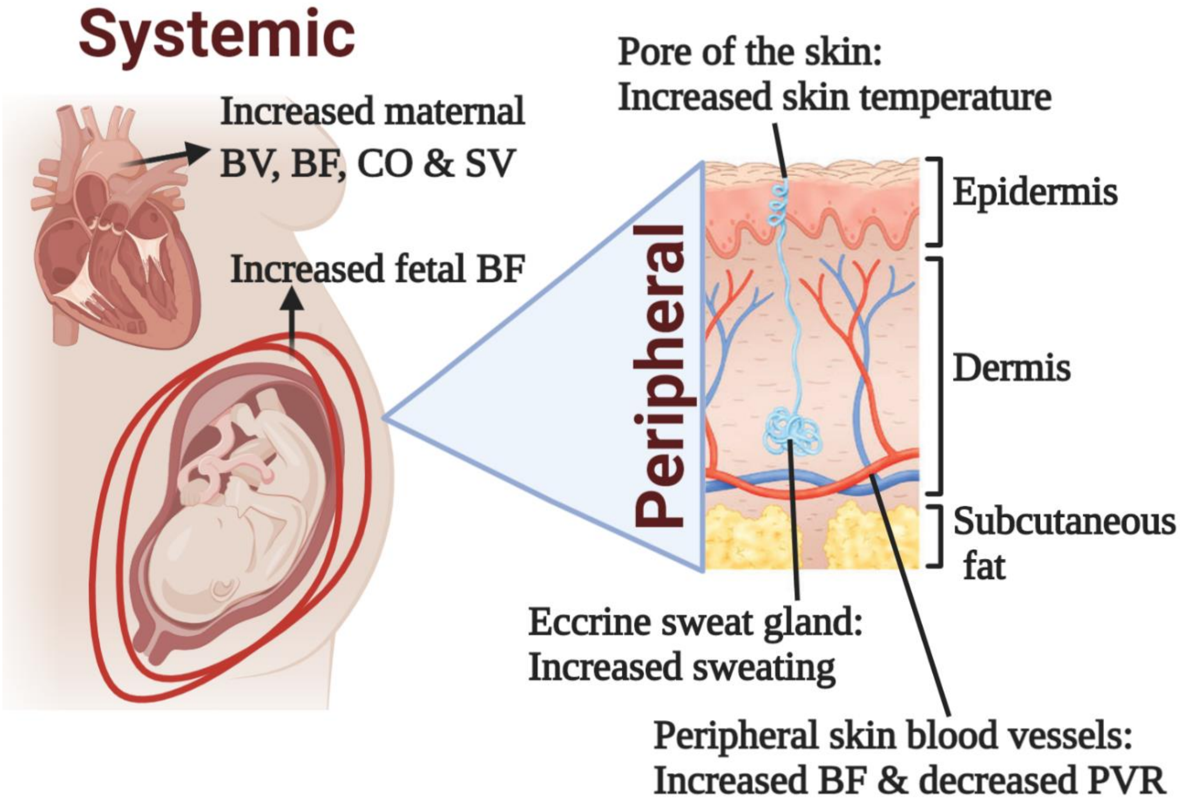

Figure 2 A schematic diagram representation of both systemic and peripheral changes that occur across pregnancy according to the current scoping review findings. BV, blood volume; BF, blood flow; CO, cardiac output; SV, stroke volume; PVR, peripheral vascular resistance. Overall, systemic, and peripheral respond similarly from early to late pregnancy.

AUTHOR CONTRIBUTION

The authors have seen and approved the manuscript.

Table 4. Outlining main findings, directions for future research and functional implications

Key findings	• Skin blood flow, stroke volume, cardiac output increases from early to late healthy pregnancy and compared to non-pregnant women/pregnant women with hypertension. • Peripheral vascular resistance decreases, and peripheral vasodilation increases from early to late pregnancy and compared to non-pregnant women/pregnant women with hypertension. • Total body sweat losses measured in weight change pre- and post- exercise/heat stress increased from early to late healthy pregnancy and compared to non-pregnant women.
Future research	• Combining local sweat rate responses using ventilated sweat capsules and weight change responses from early to late pregnancy compared to non-pregnant controls matched for total body weight. • Along with physiological measurements of heat loss, perceptual measurements using a thermal sensation scale would compliment understanding maternal-fetal protective response in thermoregulation from early to late pregnancy. • Provide culturally tailored recommendations for pregnant women, encouraging regular physical activity.
Functional implications	• Understanding and/or distinguishing the influence of weight gain separate from trimester of pregnancy on thermal responses during exercise and/or heat stress. • Potentially including a thermal sensation/comfort scale as a parameter to distinguish thermal discomfort during exercise and/or heat stress would be an additional tool to keep pregnant women safe during exercise or heat stress exposure.

References

ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. (2002). *Int J Gynaecol Obstet, 77*(1), 79-81. doi:10.1016/s0020-7292(02)80004-2

Anim-Nyame, N., Sooranna, S. R., Johnson, M. R., Gamble, J., & Steer, P. J. (2000). Resting peripheral blood flow in normal pregnancy and in pre-eclampsia. *Clin Sci (Lond), 99*(6), 505-510.

Arksey, H., & O'Malley, L. (2005). Scoping studies: towards a methodological framework. *International journal of social research methodology, 8*(1), 19-32.

Asakura, H. (2004). Fetal and neonatal thermoregulation. *Journal of Nippon Medical School, 71*(6), 360-370.

Baciuk, E. P., Pereira, R. I., Cecatti, J. G., Braga, A. F., & Cavalcante, S. R. (2008). Water aerobics in pregnancy: Cardiovascular response, labor and neonatal outcomes. *Reprod Health, 5*, 10. doi:10.1186/1742-4755-5-10

Baker, H. J., Lindsey, J. R., & Weisbroth, S. H. (1979). Preface. In H. J. Baker, J. R. Lindsey, & S. H. Weisbroth (Eds.), *The Laboratory Rat* (pp. xi-xii): Academic Press.

Barrett, L., Gaynor, D., Rendall, D., Mitchell, D., & Henzi, S. P. (2004). Habitual cave use and thermoregulation in chacma baboons (Papio hamadryas ursinus). *Journal of Human Evolution, 46*(2), 215-222. doi:https://doi.org/10.1016/j.jhevol.2003.11.005

Basu, R., Malig, B., & Ostro, B. (2010). High ambient temperature and the risk of preterm delivery. *Am J Epidemiol, 172*(10), 1108-1117. doi:10.1093/aje/kwq170

Beinder, E., Huch, A., & Huch, R. (1990). Peripheral skin temperature and microcirculatory reactivity during pregnancy. A study with thermography. *J Perinat Med, 18*(5), 383-390. doi:10.1515/jpme.1990.18.5.383

Bicca-Marques, J. C., & Calegaro-Marques, C. (1998). Behavioral thermoregulation in a sexually and developmentally dichromatic neotropical primate, the black-and-gold howling monkey (Alouatta caraya). *Am J Phys Anthropol, 106*(4), 533-546. doi:10.1002

Brearley, A. L., Sherburn, M., Galea, M. P., & Clarke, S. J. (2015). Pregnant women maintain body temperatures within safe limits during moderate-intensity aqua-aerobic classes conducted in pools heated up to 33 degrees Celsius: an observational study. *J Physiother, 61*(4), 199-203. doi:10.1016/j.jphys.2015.08.004

Campos, F. A., & Fedigan, L. M. (2009). Behavioral adaptations to heat stress and water scarcity in white-faced capuchins (Cebus capucinus) in Santa Rosa National Park, Costa Rica. *Am J Phys Anthropol, 138*(1), 101-111. doi:10.1002/ajpa.20908

Cankar, K., Potocnik, N., & Strucl, M. (2010). Alteration of skin laser-Doppler flux response to local cooling in gestational hypertension. *Clin Auton Res, 20*(3), 183-190. doi:10.1007/s10286-009-0050-1

Cena, K., & de Dear, R. (2001). Thermal comfort and behavioural strategies in office buildings located in a hot-arid climate. *Journal of Thermal Biology, 26*(4), 409-414. doi:https://doi.org/10.1016/S0306-4565(01)00052-3

Chandler, K. D., & Bell, A. W. (1981). Effects of maternal exercise on fetal and maternal respiration and nutrient metabolism in the pregnant ewe. *J Dev Physiol, 3*(3), 161-176.

Chapman, A. B., Abraham, W. T., Zamudio, S., Coffin, C., Merouani, A., Young, D., Schrier, R. W. (1998). Temporal relationships between hormonal and hemodynamic changes in early human pregnancy. *Kidney Int, 54*(6), 2056-2063. doi:10.1046/j.1523-1755.1998.00217.x

Clapp, J. F. (2006). Influence of endurance exercise and diet on human placental development and fetal growth. *Placenta, 27*(6-7), 527-534. doi:10.1016/j.placenta.2005.07.010

Clapp, J. F., 3rd. (1980). Acute exercise stress in the pregnant ewe. *Am J Obstet Gynecol, 136*(4), 489-494. doi:10.1016/0002-9378(80)90676-6

Clapp, J. F., 3rd. (1991). The changing thermal response to endurance exercise during pregnancy. *Am J Obstet Gynecol, 165*(6 Pt 1), 1684-1689. doi:10.1016/0002-9378(91)90015-j

Clapp, J. F., 3rd, & Capeless, E. (1997). Cardiovascular function before, during, and after the first and subsequent pregnancies. *Am J Cardiol, 80*(11), 1469-1473. doi:10.1016/s0002-9149(97)00738-8

Clapp, J. F., 3rd, Stepanchak, W., Tomaselli, J., Kortan, M., & Faneslow, S. (2000). Portal vein blood flow-effects of pregnancy, gravity, and exercise. *Am J Obstet Gynecol, 183*(1), 167-172. doi:10.1067/mob.2000.105902

Clapp, J. F., 3rd, Wesley, M., & Sleamaker, R. H. (1987). Thermoregulatory and metabolic responses to jogging prior to and during pregnancy. *Med Sci Sports Exerc, 19*(2), 124-130.

Cramer, M. N., & Jay, O. (2016). Biophysical aspects of human thermoregulation during heat stress. *Auton Neurosci, 196*, 3-13. doi:10.1016/j.autneu.2016.03.001

Curet, L. B., Orr, J. A., Rankin, H. G., & Ungerer, T. (1976). Effect of exercise on cardiac output and distribution of uterine blood flow in pregnant ewes. *J Appl Physiol, 40*(5), 725-728. doi:10.1152/jappl.1976.40.5.725

Davenport, M. H., Ruchat, S. M., Mottola, M. F., Davies, G. A., Poitras, V. J., Gray, C. E., . Zehr, L. (2018). 2019 Canadian Guideline for Physical Activity Throughout Pregnancy: Methodology. *J Obstet Gynaecol Can, 40*(11), 1468-1483. doi:10.1016/j.jogc.2018.09.004

Davenport, M. H., Ruchat, S. M., Poitras, V. J., Jaramillo Garcia, A., Gray, C. E., Barrowman, N., Mottola, M. F. (2018). Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. *Br J Sports Med, 52*(21), 1367-1375. doi:10.1136/bjsports-2018-099355

Davenport, M. H., Ruchat, S. M., Sobierajski, F., Poitras, V. J., Gray, C. E., Yoo, C., Mottola, M. F. (2019). Impact of prenatal exercise on maternal harms, labour and delivery outcomes: a systematic review and meta-analysis. *Br J Sports Med, 53*(2), 99-107. doi:10.1136/bjsports-2018-099821

Davenport, M. H., Yoo, C., Mottola, M. F., Poitras, V. J., Jaramillo Garcia, A., Gray, C. E., . Ruchat, S. M. (2019). Effects of prenatal exercise on incidence of congenital anomalies and hyperthermia: a systematic review and meta-analysis. *Br J Sports Med, 53*(2), 116-123. doi:http://dx.doi.org/10.1136/bjsports-2018-099653

Davies, G. A., Wolfe, L. A., Mottola, M. F., MacKinnon, C., Arsenault, M. Y., Bartellas, E., Trudeau, F. (2003). Exercise in pregnancy and the postpartum period. *J Obstet Gynaecol Can, 25*(6), 516-529. doi:10.1016/s1701-2163(16)30313-9

Downey, J. (2008). *Perceptions and experiences of women who continue vigorous physical activity during pregnancy.* (MR42008 M.Sc.), Memorial University of Newfoundland (Canada), Ann Arbor.

Duncan, L., & Pillay, N. (2013). Shade as a thermoregulatory resource for captive chimpanzees. *Journal of Thermal Biology, 38*, 169–177. doi:10.1016/j.jtherbio.2013.02.009

Dunlap, S. R. (2003). *Thermoregulation in shallow water aquatic exercise during second trimester pregnancy.* (3110334 Ph.D.), University of Idaho, Ann Arbor.

Edwards, M. J., Saunders, R. D., & Shiota, K. (2003). Effects of heat on embryos and foetuses. *Int J Hyperthermia, 19*(3), 295-324. doi:10.1080/0265673021000039628

Ejidokun, O. O. (2000). Community attitudes to pregnancy, anaemia, iron and folate supplementation in urban and rural Lagos, south-western Nigeria. *Midwifery, 16*(2), 89-95. doi:10.1054/midw.1999.0196

Erkkola, R. U., Pirhonen, J. P., & Kivijärvi, A. K. (1992). Flow velocity waveforms in uterine and umbilical arteries during submaximal bicycle exercise in normal pregnancy. *Obstet Gynecol, 79*(4), 611-615.

Evenson, K. R., Barakat, R., Brown, W. J., Dargent-Molina, P., Haruna, M., Mikkelsen, E. M., . . . Yeo, S. (2014). Guidelines for Physical Activity during Pregnancy: Comparisons From Around the World. *American journal of lifestyle medicine, 8*(2), 102-121. doi:10.1177/1559827613498204

Fawer, R., Dettling, A., Weihs, D., Welti, H., & Schelling, J. L. (1978). Effect of the menstrual cycle, oral contraception and pregnancy on forearm blood flow, venous distensibility and clotting factors. *Eur J Clin Pharmacol, 13*(4), 251-257. doi:10.1007/bf00716359

Franklin, A., Mishtal, J., Johnson, T., & Simms-Cendan, J. (2017). Rowers' Self-Reported Behaviors, Attitudes, and Safety Concerns Related to Exercise, Training, and Competition During Pregnancy. *Cureus, 9*(8), e1534-e1534. doi:10.7759/cureus.1534

Gagge, A. P., & Gonzales, R. R. (1996). Mechanisms of heat exchange In Fregley MJ & Blatteis CM (Eds.), *Handbook of Physiology. Section 4: Environmental Physiology* (pp. 45-84). New York, NY: Oxford University press.

Gagge, A. P., Stolwijk, J. A., & Saltin, B. (1969). Comfort and thermal sensations and associated physiological responses during exercise at various ambient temperatures. *Environ Res, 2*(3), 209-229. doi:10.1016/0013-9351(69)90037-1

Graham, J. M., Jr., Edwards, M. J., & Edwards, M. J. (1998). Teratogen update: gestational effects of maternal hyperthermia due to febrile illnesses and resultant patterns of defects in humans. *Teratology, 58*(5), 209-221. doi:10.1002/(sici)1096-9926(199811)58:5<209::Aid-tera8>3.0.Co;2-q

Hammel, H. T. (1968). Regulation of internal body temperature. *Ann Rev Physiol, 30*, 641-710.

Hankenson, F. C., Marx, J. O., Gordon, C. J., & David, J. M. (2018). Effects of Rodent Thermoregulation on Animal Models in the Research Environment. *Comparative medicine, 68*(6), 425-438. doi:10.30802/AALAS-CM-18-000049

Hartgill, T. W., Bergersen, T. K., & Pirhonen, J. (2011). Core body temperature and the thermoneutral zone: a longitudinal study of normal human pregnancy. *Acta Physiol (Oxf), 201*(4), 467-474. doi:10.1111/j.1748-1716.2010.02228.x

Hartmann, S., & Bung, P. (1999). Physical exercise during pregnancy--physiological considerations and recommendations. *J Perinat Med, 27*(3), 204-215. doi:10.1515/jpm.1999.029

Havenith, G. (2005). Temperature Regulation, Heat Balance and Climatic Stress. In W. Kirch, R. Bertollini, & B. Menne (Eds.), *Extreme Weather Events and Public Health Responses* (pp. 69-80). Berlin, Heidelberg: Springer Berlin Heidelberg.

Iacobaeus, C., Andolf, E., Thorsell, M., Bremme, K., Jörneskog, G., Östlund, E., & Kahan, T. (2017). Longitudinal study of vascular structure and function during normal pregnancy. *Ultrasound Obstet Gynecol, 49*(1), 46-53. doi:10.1002/uog.17326

Jeffreys, R. M., Stepanchak, W., Lopez, B., Hardis, J., & Clapp, J. F., 3rd. (2006). Uterine blood flow during supine rest and exercise after 28 weeks of gestation. *Bjog, 113*(11), 1239-1247. doi:10.1111/j.1471-0528.2006.01056.x

Jones, R. L., Botti, J. J., Anderson, W. M., & Bennett, N. L. (1985). Thermoregulation during aerobic exercise in pregnancy. *Obstet Gynecol, 65*(3), 340-345.

Karjalainen, S. (2012). Thermal comfort and gender: a literature review. *Indoor Air, 22*(2), 96-109. doi:10.1111/j.1600-0668.2011.00747.x

Katz, V. L. (1996). Water exercise in pregnancy. *Semin Perinatol, 20*(4), 285-291. doi:10.1016/s0146-0005(96)80021-8

Kingma, B., Frijns, A., & van Marken Lichtenbelt, W. (2012). The thermoneutral zone: Implications for metabolic studies. *Frontiers in bioscience (Elite edition), 4*, 1975-1985. doi:10.2741/E518

Larsson, L., & Lindqvist, P. G. (2005). Low-impact exercise during pregnancy--a study of safety. *Acta Obstet Gynecol Scand, 84*(1), 34-38. doi:10.1111/j.0001-6349.2005.00696.x

Lindqvist, P. G., Marsal, K., Merlo, J., & Pirhonen, J. P. (2003). Thermal response to submaximal exercise before, during and after pregnancy: a longitudinal study. *J Matern Fetal Neonatal Med, 13*(3), 152-156. doi:10.1080/jmf.13.3.152.156

Lotgering, F. K., Gilbert, R. D., & Longo, L. D. (1983). Exercise responses in pregnant sheep: blood gases, temperatures, and fetal cardiovascular system. *J Appl Physiol Respir Environ Exerc Physiol, 55*(3), 842-850. doi:10.1152/jappl.1983.55.3.842

Macaulay, J. H., Randall, N. R., Bond, K., & Steer, P. J. (1992). Continuous monitoring of fetal temperature by noninvasive probe and its relationship to maternal temperature, fetal heart rate, and cord arterial oxygen and pH. *Obstet Gynecol, 79*(3), 469-474. doi:10.1097/00006250-199203000-00029

Majolo, B., McFarland, R., Young, C., & Qarro, M. (2013). The Effect of Climatic Factors on the Activity Budgets of Barbary Macaques. *International Journal of Primatology, 34*, 500-514. doi:10.1007/s10764-013-9678-8

Marks, L. E., & Gonzalez, R. R. (1974). Skin temperature modifies the pleasantness of thermal stimuli. *Nature, 247*(5441), 473-475. doi:10.1038/247473a0

McFarland, R., Barrett, L., Costello, M. A., Fuller, A., Hetem, R. S., Maloney, S. K., Henzi, P. S. (2019). Keeping cool in the heat: Behavioral thermoregulation and body temperature patterns in wild vervet monkeys. *Am J Phys Anthropol*. doi:10.1002/ajpa.23962

McMurray, R. G., Berry, M. J., Katz, V. L., Graetzer, D. G., & Cefalo, R. C. (1990). The thermoregulation of pregnant women during aerobic exercise in the water: a longitudinal approach. *Eur J Appl Physiol Occup Physiol, 61*(1-2), 119-123. doi:10.1007/bf00236704

McMurray, R. G., & Katz, V. L. (1990). Thermoregulation in pregnancy. Implications for exercise. *Sports Med, 10*(3), 146-158. doi:10.2165/00007256-199010030-00002

McMurray, R. G., Katz, V. L., Meyer-Goodwin, W. E., & Cefalo, R. C. (1993). Thermoregulation of pregnant women during aerobic exercise on land and in the water. *Am J Perinatol, 10*(2), 178-182. doi:10.1055/s-2007-994656

Metcalfe, J., & Ueland, K. (1974). Maternal cardiovascular adjustments to pregnancy. *Prog Cardiovasc Dis, 16*(4), 363-374. doi:10.1016/0033-0620(74)90028-0

Miller, M. W., Nyborg, W. L., Dewey, W. C., Edwards, M. J., Abramowicz, J. S., & Brayman, A. A. (2002). Hyperthermic teratogenicity, thermal dose and diagnostic ultrasound during pregnancy: implications of new standards on tissue heating. *Int J Hyperthermia, 18*(5), 361-384. doi:10.1080/02656730210146890

Mitchell, D., Snelling, E. P., Hetem, R. S., Maloney, S. K., Strauss, W. M., & Fuller, A. (2018). Revisiting concepts of thermal physiology: Predicting responses of mammals to climate change. *J Anim Ecol, 87*(4), 956-973. doi:10.1111/1365-2656.12818

Moore, D. H., Jarrett, J. C., 2nd, & Bendick, P. J. (1988). Exercise-induced changes in uterine artery blood flow, as measured by Doppler ultrasound, in pregnant subjects. *Am J Perinatol, 5*(2), 94-97. doi:10.1055/s-2007-999663

Mottola, M. F., Davenport, M. H., Ruchat, S. M., Davies, G. A., Poitras, V. J., Gray, C. E., Zehr, L. (2018). 2019 Canadian guideline for physical activity throughout pregnancy. *Br J Sports Med, 52*(21), 1339-1346. doi:10.1136/bjsports-2018-100056

Myhrman, P., Jansson, I., & Lundgren, Y. (1980). Skin blood flow in normal pregnancy measured by venous occlusion plethysmography of the hand. *Acta Obstet Gynecol Scand, 59*(2), 107-110. doi:10.3109/00016348009154624

Nakamura, M., Yoda, T., Crawshaw, L. I., Yasuhara, S., Saito, Y., Kasuga, M., Kanosue, K. (2008). Regional differences in temperature sensation and thermal comfort in humans. *J Appl Physiol (1985), 105*(6), 1897-1906. doi:10.1152/japplphysiol.90466.2008

Newton, E. R., & May, L. (2017). Adaptation of Maternal-Fetal Physiology to Exercise in Pregnancy: The Basis of Guidelines for Physical Activity in Pregnancy. *Clinical medicine insights. Women's health, 10*, 1179562X17693224-11179562X17693224. doi:10.1177/1179562X17693224

Ngongalah, L., Rankin, J., Rapley, T., Odeniyi, A., Akhter, Z., & Heslehurst, N. (2018). Dietary and physical activity behaviours in African migrant women living in high income countries: A systematic review and framework synthesis. *Nutrients, 10*(8). doi:10.3390/nu10081017

O'Neill, M. E. (1996). Maternal rectal temperature and fetal heart rate responses to upright cycling in late pregnancy. *Br J Sports Med, 30*(1), 32-35. doi:10.1136/bjsm.30.1.32

Ohlmann, P., Jung, F., Mrowietz, C., Alt, T., Alt, S., & Schmidt, W. (2001). Peripheral microcirculation during pregnancy and in women with pregnancy induced hypertension. *Clin Hemorheol Microcirc, 24*(3), 183-191.

Pellerin, N., & Candas, V. (2003). Combined effects of temperature and noise on human discomfort. *Physiology & Behavior, 78*(1), 99-106. doi:https://doi.org/10.1016/S0031-9384(02)00956-3

Peters, M. D. J., Marnie, C., Tricco, A. C., Pollock, D., Munn, Z., Alexander, L., Khalil, H. (2020). Updated methodological guidance for the conduct of scoping reviews. *JBI Evidence Synthesis, 18*(10), 2119-2126. doi:10.11124/jbies-20-00167

Petrov Fieril, K., Glantz, A., & Fagevik Olsen, M. (2016a). Hemodynamic responses to single sessions of aerobic exercise and resistance exercise in pregnancy. *Acta Obstet Gynecol Scand, 95*(9), 1042-1047. doi:10.1111/aogs.12899

Pivarnik, J. M., Lee, W., Clark, S. L., Cotton, D. B., Spillman, H. T., & Miller, J. F. (1990). Cardiac output responses of primigravid women during exercise determined by the direct Fick technique. *Obstet Gynecol, 75*(6), 954-959.

Power, G. G. (1989). Biology of temperature: the mammalian fetus. *J Dev Physiol, 12*(6), 295-304.

Prozesky, O. P. M. (1963). Body Temperature of Birds in Relation to Nesting Habits. *Nature, 197*(4865), 401-402. doi:10.1038/197401b0

Ravanelli, N., Casasola, W., English, T., Edwards, K. M., & Jay, O. (2019). Heat stress and fetal risk. Environmental limits for exercise and passive heat stress during pregnancy: a systematic review with best evidence synthesis. *Br J Sports Med, 53*(13), 799-805. doi:10.1136/bjsports-2017-097914

Robertshaw, D. (2006). Mechanisms for the control of respiratory evaporative heat loss in panting animals. *Journal of Applied Physiology, 101*(2), 664-668.

Ruchat, S. M., Mottola, M. F., Skow, R. J., Nagpal, T. S., Meah, V. L., James, M.,Davenport, M. H. (2018). Effectiveness of exercise interventions in the prevention of excessive gestational weight gain and postpartum weight retention: a systematic review and meta-analysis. *Br J Sports Med, 52*(21), 1347-1356. doi:10.1136/bjsports-2018-099399

Salvesen, K., Hem, E., & Sundgot-Borgen, J. (2012). Fetal wellbeing may be compromised during strenuous exercise among pregnant elite athletes. *Br J Sports Med, 46*(4), 279-283. doi:10.1136/bjsm.2010.080259

Schellen, L., Loomans, M. G. L. C., de Wit, M. H., Olesen, B. W., & Lichtenbelt, W. D. v. M. (2012). The influence of local effects on thermal sensation under non-uniform environmental conditions — Gender differences in thermophysiology, thermal comfort and productivity during convective and radiant cooling. *Physiology & Behavior, 107*(2), 252-261. doi:https://doi.org/10.1016/j.physbeh.2012.07.008

Schröder, H. J., & Power, G. G. (1994). Increase of fetal arterial blood temperature by reduction of umbilical blood flow in chronically instrumented fetal sheep. *Pflugers Arch, 427*(1-2), 190-192. doi:10.1007/bf00585962

Schröder, H. J., & Power, G. G. (1997). Engine and radiator: fetal and placental interactions for heat dissipation. *Exp Physiol, 82*(2), 403-414. doi:10.1113/expphysiol.1997.sp004035

Sillero-Quintana, M., Conde-Pascual, E., Gomez-Carmona, P. M., Fernandez-Cuevas, I., & Garcia-Pastor, T. (2012). Effect of Yoga and Swimming on body temperature of pregnant women. *Thermology International, 22*(3), 143-149.

Simoes, R., Vardasca, R., & Nogueira-Silva, C. (2012). Thermal skin reference values in healthy late pregnancy. *Journal of Thermal Biology, 37*(8), 608-614. doi:http://dx.doi.org/10.1016/j.jtherbio.2012.07.006

Soultanakis-Aligianni, H. N. (2003). Thermoregulation during exercise in pregnancy. *Clin Obstet Gynecol, 46*(2), 442-455. doi:10.1097/00003081-200306000-00023

Soultanakis, H. N. (2016). Aquatic Exercise and Thermoregulation in Pregnancy. *Clin Obstet Gynecol, 59*(3), 576-590. doi:10.1097/grf.0000000000000209

Spatling, L., Fallenstein, F., Huch, A., Huch, R., & Rooth, G. (1992). The variability of cardiopulmonary adaptation to pregnancy at rest and during exercise. *Br J Obstet Gynaecol, 99 Suppl 8*, 1-40.

Stark, M. J., Dierkx, L., Clifton, V. L., & Wright, I. M. R. (2006). Alterations in the Maternal Peripheral Microvascular Response in Pregnancies Complicated by Preeclampsia and the Impact of Fetal Sex. *Journal of the Society for Gynecologic Investigation, 13*(8), 573-578. doi:http://dx.doi.org/10.1016/j.jsgi.2006.06.006

Stelzner, J. K., & Hausfater, G. (1986). Posture, microclimate, and thermoregulation in yellow baboons. *Primates, 27*(4), 449-463. doi:10.1007/BF02381890

Szymanski, L. M., & Kogutt, B. K. (2018). Uterine Artery Doppler Velocimetry During Individually Prescribed Exercise in Pregnancy. *Obstet Gynecol, 132*(4), 1026-1032. doi:10.1097/aog.0000000000002779

Tan, E. K., & Tan, E. L. (2013). Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol, 27*(6), 791-802. doi:10.1016/j.bpobgyn.2013.08.001

Thornburg, K. L., Jacobson, S. L., Giraud, G. D., & Morton, M. J. (2000). Hemodynamic changes in pregnancy. *Semin Perinatol, 24*(1), 11-14. doi:10.1016/s0146-0005(00)80047-6

Tuffnell, D., Buchan, P., Albert, D., & Tyndale-biscoe, S. (2009). Fetal heart rate responses to maternal exercise, increased maternal temperature and maternal circadian variation. *Journal of Obstetrics & Gynaecology, 10*, 387-391. doi:10.3109/01443619009151222

Tuffnell, D. J., Buchan, P. C., Albert, D., & Tyndale-biscoe, S. (1990). Fetal heart rate responses to maternal exercise, increased maternal temperature and maternal circadian variation. *Journal of Obstetrics and Gynaecology, 10*(5), 387-391. doi:10.3109/01443619009151222

Tur, E., Tamir, A., & Guy, R. H. (1992a). Cutaneous blood flow in gestational hypertension and normal pregnancy. *J Invest Dermatol, 99*(3), 310-314. doi:10.1111/1523-1747.ep12616649

Tur, E., Tamir, A., & Guy, R. H. (1992b). Cutaneous blood flow in gestational hypertension and normal pregnancy. *Journal of Investigative Dermatology, 99*(3), 310-314.

Vaha-Eskeli, K., Erkkola, R., & Seppanen, A. (1991). Is the heat dissipating ability enhanced during pregnancy? *Eur J Obstet Gynecol Reprod Biol, 39*(3), 169-174. doi:10.1016/0028-2243(91)90053-n

Vähä-Eskeli, K., Erkkola, R., & Seppänen, A. (1991). Is the heat dissipating ability enhanced during pregnancy? *Eur J Obstet Gynecol Reprod Biol, 39*(3), 169-174. doi:10.1016/0028-2243(91)90053-n

Vähä-Eskeli, K. K., Erkkola, R. U., Seppänen, A., Poranen, A. K., & Säteri, U. (1991). Haemodynamic response to moderate thermal stress in pregnancy. *Ann Med, 23*(2), 121-126. doi:10.3109/07853899109148035

Wang, D., Zhang, H., Arens, E., & Huizenga, C. (2007). Observations of upper-extremity skin temperature and corresponding overall-body thermal sensations and comfort. *Building and Environment, 42*(12), 3933-3943. doi:https://doi.org/10.1016/j.buildenv.2006.06.035

Wulandari, L. P., & Klinken Whelan, A. (2011). Beliefs, attitudes and behaviours of pregnant women in Bali. *Midwifery, 27*(6), 867-871. doi:10.1016/j.midw.2010.09.005

Zhang, H., Arens, E., Huizenga, C., & Han, T. (2010). Thermal sensation and comfort models for non-uniform and transient environments, part II: Local comfort of individual body parts. *Building and Environment - BLDG ENVIRON, 45*, 389-398. doi:10.1016/j.buildenv.2009.06.015

Ziskin, M. C., & Morrissey, J. (2011). Thermal thresholds for teratogenicity, reproduction, and development. *Int J Hyperthermia, 27*(4), 374-387. doi:10.3109/02656736.2011.553769

CHAPTER 6

DISCUSSION AND GENERAL CONCLUSIONS OF THE THESIS

Overall, the findings of this thesis provide insight into heat balance across pregnancy, including the determinants that influence heat production responses (i.e., body weight & exercise intensity) and a comprehensive review of the current literature regarding heat loss mechanisms (i.e., evaporative, and dry heat loss). The experimental design of *Study 1 & Study 2* included a cross-sectional inter-individual comparison of pregnant women at different pregnancy-timepoints (i.e., early, middle and late stages of pregnancy) either matched (MW) or not matched (NWM) for total body weight. *Study 1* assessed the resting metabolic rate during pregnancy and revealed pregnant women matched for total body weight at early, middle to late pregnancy timepoints responded similarly in heat production (kJ & kJ/min) and heart rate (bpm). On the other hand, in the group not matched for total body weight between pregnancy timepoints, the heat production and heart rate responses at rest corresponded to the changes in total body weight (i.e., as total body weight increased so did resting heat production and heart rate). The outcomes in Study 1 reveal that total body mass weight independent of stage of pregnancy influences the physiological responses of heat production and heart rate. The question remained whether these responses continued during weight-bearing exercise. Therefore, the experimental design of *Study 2* was established to control for weight during weight-bearing exercise across pregnancy timepoints on heat production, heart rate, and the subjective ratings of perceived exertion.

The protocol in *Study 2* was used to compare both physiological and subjective measurements during an incremental weight-bearing walking test. The incremental design of the test was set to define a potential threshold in which differences would occur between groups as the intensity of exercise increased from low- to moderate- (i.e., 50-70% Maximal HR) to vigorous-

(i.e., 70-85% Maximal HR) between pregnancy timepoints in both WM and NWM groups. The cut-off to stop exercising was 85% Maximal HR. The physiological outcomes of heat production and heart rate followed that of *Study 1*. In *Study 2* the subjective measurements of perceived exertion (RPE) corresponded to the physiological outcomes only in the weight-matched group. An interesting and unexpected finding was that the subjective measurement of RPE in the non-weight-matched group did not differ between pregnancy timepoints. The perceptual measurements did not follow the same trend as the physiological outcomes of heat production and heart rate. Moreover, the timepoint of pregnancy on its own did not impact the physiological responses at rest or during exercise from low to moderate intensity. The outcomes of *Study* 2 suggest that both weight and intensity of exercise influence physiological measurements of heat production and heart rate. Therefore, future work comparing thermoregulatory responses across pregnancy should account for the differences in total body weight and ensure participants are exercising at the same intensity of exercise. The combination of *Study 1* and *Study 2* addresses the metabolic heat production side of the heat balance equation. However, the question remains: how does the progression of pregnancy influence heat loss responses? Before the start of the global COVID-19 pandemic early in year 2020, I was ready to start an actual physiological measurement study (*Study 3)*, which was designed to measure both evaporative (i.e., sweat loss in body weight change and sweat rate using ventilated sweat capsules) and dry (i.e., skin blood flow measurements using laser Doppler flowmetry) heat loss responses across pregnancy using a similar experimental design as that established in *Study 1 and Study 2*. Given the pandemic-related circumstances, *Study 3* was put on hold and replaced by a scoping review mapping existing literature on physiological, perceptual, and behavioural heat loss-related responses in pregnant women, and characterizing results accordingly.

In *Study 3*, the scoping review summarized human studies that measured heat loss responses during pregnancy. The level of understanding of core temperature responses in pregnant women (Jones *et al.*, 1985; Clapp *et al.*, 1987; McMurray *et al.*, 1990; Clapp, 1991; Vaha-Eskeli *et al.*, 1991; McMurray *et al.*, 1993; O'Neill, 1996; Lindqvist *et al.*, 2003; Larsson & Lindqvist, 2005; Clapp, 2006; Tuffnell *et al.*, 2009; Brearley *et al.*, 2015; Petrov Fieril *et al.*, 2016a) was not met correspondingly with the same understanding in heat loss responses (Curet *et al.*, 1976; Clapp, 1980; Chandler & Bell, 1981; Lotgering *et al.*, 1983; Power, 1989; Schröder & Power, 1994; Edwards *et al.*, 2003). Typically, assumptions were made regarding heat loss responses in pregnant women based on the results of a small set of animal studies (Prozesky, 1963; Baker *et al.*, 1979; Edwards *et al.*, 2003). Given the minimal data and disparate findings in human studies regarding heat loss responses across pregnancy, a scoping review was considered the most appropriate type of review to map findings and inform research gaps that can be addressed in future investigations. The main results of this scoping review can be summarized in terms of dry heat loss related to i) cardiovascular responses; there exists an increase from early to late pregnancy, and evaporative heat loss related to ii) sweating in the very limited number of studies suggest that there exists an increase of sweating response from early to late pregnancy. The limited measurements of sweating, and suboptimal experimental designs to demonstrate the influence of pregnancy on heat loss suggests a need for future thermoregulatory related research design using a fixed heat production protocol across pregnancy timepoints and measuring heat loss as a rate in sweating (i.e., using ventilated sweat capsules), skin blood flow, and overall sweat loss pre-and post-exercise. Another major outcome from the scoping review revealed that throughout exercise, the addition of a subjective measure of rating of perceived exertion, thermal sensation, and thermal comfort would be valuable in providing insight into the relationship between the physiological and perceptual strain during exercise throughout pregnancy. Based on the evidence (or lack of) uncovered in the scoping review, there is a significant gap in our knowledge of evaporative (i.e., sweat) and dry (i.e., skin blood flow) heat loss mechanisms across pregnancy timepoints during exercise, illustrating the need to measure heat loss mechanisms throughout pregnancy as intended prior to the COVID-19 pandemic. The combination of a fixed heat production to measure heat loss and core temperature outcomes would satisfy the requirements of the heat balance equation and as such understanding of thermoregulatory functions throughout pregnancy.

Perspectives and Considerations

An important environmental parameter not considered in this current thesis nor in any study investigating thermoregulatory responses between pregnancy timepoints is the consideration of compensable versus non-compensable conditions (Gagnon & Kenny, 2012; Cramer & Jay, 2016). The impetus of evaporation is the vapour pressure gradient of sweat saturated skin surface and the absolute humidity of the ambient air (also influenced by air velocity), that together influence the percentage of skin wettedness (Candas *et al.*, 1979a, b). Skin wettedness represents a theoretical fraction of body surface area that, if fully covered by sweat, would result in a given rate of evaporation from the skin and the maximum capacity of evaporation (Candas *et al.*, 1979a, b), reflecting the limitation of evaporative heat loss imposed by the environment from a fully 'wet' skin surface. The maximum evaporation capacity is a function of the maximum skin wettedness (Candas *et al.*, 1979a, b). A commonly used term to express evaporation and skin wettedness in terms of heat balance requirements is 'evaporative requirement'(Candas *et al.*, 1979a, b). The skin wettedness essential for heat balance represents the portion of the skin surface that theoretically should be enclosed to attain evaporative requirements for heat balance (Candas *et al.*, 1979a, b). The maximum skin wettedness depends on heat acclimation, aerobic fitness level and various physiological paraments that could affect the ratio at which skin wettedness results in inefficient sweating creating an ‘uncompensable’ environment (i.e., not achieving heat balance) (Berglund & Gonzalez, 1977). Considering the body morphology changes as pregnancy progresses, a given environment may be considered compensable early on in pregnancy and become uncompensable at end stages of pregnancy.

The contribution of body heat capacity in core temperature change at a certain rate of heat storage is determined by the specific heat of body tissue (Cramer & Jay, 2016). The body's average heat capacity is based on thermal properties of individual tissue types and the variation in relative contribution of bone density, lean and adipose tissue, including total body mass (Passmore & Durnin, 1955; Wyndham & Atkins, 1968; Stolwijk & Hardy, 2011). The specific heat of body fat amounts to about 2.51 J/g, whereas that of the other tissues (skeleton, skin, muscle, blood., etc., combined) is on average 3.65 J/g (Stolwijk & Hardy, 2011). The resistance to heat transport from core to the skin is created by muscle, adipose and skin (Nadel *et al.*, 1971; Havenith & van Middendorp, 1990; Havenith *et al.*, 1998; Havenith, 2001; Stolwijk & Hardy, 2011). Individuals with higher adiposity would be expected to have greater changes in core temperature for a given change in body heat content and mass (Nadel *et al.*, 1971; Havenith & van Middendorp, 1990; Havenith *et al.*, 1998; Havenith, 2001; Stolwijk & Hardy, 2011; Cramer & Jay, 2016). A study compared core temperature and sweating responses to exercise at a fixed heat production of 550 W between groups of high (~32%) or low (~11%) adiposity but matched for total body mass (kg) (Dervis *et al.*, 2016). The authors reported a greater core temperature change in the high-adiposity group without any changes in whole-body or local sweat rates (Dervis *et al.*, 2016). Although the higher core temperature change may be attributed to the lower average specific heat capacity of body tissue in low-adiposity (3.65 kJ Kg min) versus high adiposity (3.49 kJ kg min) individuals, the absence of any difference in sweat rates suggests that adiposity *per se* independently influences sudomotor control. The body composition changes in pregnancy and vast differences in the ratio of fat-mass and fat-free mass at different pregnancy timepoints may influence the overall specific heat in pregnant women. Therefore, the combination of changing body surface area and specific body heat contribution to the physiological and physical changes in pregnancy influences thermoregulatory function.

In this thesis, the NWM groups differed in weight between pregnancy timepoints, T1 = 65.4 ± 8.9, T2 = 74.8 ± 9.7, T3 = 79.9 ± 8.9 kg, essentially an approximate difference of ~15 kg. The body composition in terms of fat-mass and fat-free mass were not considered, and consequently, we were unable to consider these variables in the measurements of heat production and heart rate at rest and during exercise steadily increased across pregnancy. Within the range of gestational weight gain, maternal fat-mass has been reported to be the most variable component (Lederman *et al.*, 1997; Most *et al.*, 2018). Unfortunately, there is limited data available in which body composition measured across pregnancy to differentiate the ratio of fat-mass and fat-free mass, although one study demonstrated a linear increase in fat mass throughout pregnancy at a rate of approximately 2 kg per trimester (Butte *et al.*, 2003). Current gestational weight gain guidelines (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009) do not include recommendations specifically for fat-mass and fat-free mass; however, several studies indicated that among the pregnant women that gained weight within the guidelines (I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines, 2009), changes in fat-free mass remained constant, with most of the variability attributed to fat-mass (Lederman *et al.*, 1997; Most *et al.*, 2018). The relationship between body composition and heat capacity of tissues throughout pregnancy would illustrate the specific contribution of fat-mass and fat-free mass on the variability in thermoregulatory responses with increasing gestational weight gain.

Future Work

As previously mentioned, the intention of *Study 3* was an actual physiological measurement study designed to measure heat loss in pregnant women accounting for total body weight and exercise intensity, brefore the onset of the COVID-19 pandemic and associated restrictions. The REB-approved study (H-12-19-5087) includes a cross-sectional inter-individual comparison of pregnant women in early, middle, and late pregnancy timepoints, matched for total body weight, height, maternal age, and BMI. The experimental protocol consists 3 stages that will take place in two different environments, one above and one below resting skin temperature (~ 34°C). The first stage is a resting period, followed by the second stage, including a steady-state moderate-intensity weight-bearing treadmill walking protocol, to enable achieving heat balance. Finally, considering there is minimal data regarding recovery thermoregulatory responses, especially in pregnancy, we will include ~ 20 minutes for a recovery period. For all 3 stages, we will measure and evaluate both physiological and perceptual mechanisms of heat loss and heat production including sweat rate (using ventilated sweat capsules, weight change and sweat patches), sweat gland density, skin blood flow, skin temperature, rectal temperature, heat production, heart rate, blood pressure, thermal comfort/sensation, and rating of perceived exertion. Using the results of this study design, we will be able to isolate how different pregnancy timepoints influence heat loss at rest, during exercise, and active recovery in two different ambient conditions. This study will discern the influence of body weight and pregnancy timepoints on heat loss onset threshold, sensitivity, and capacity if participants reach an uncompensable output (i.e., sweating does not continue to rise with increasing core temperature). Based on the current literature, we would anticipate that later in pregnancy the heat loss mechanisms of onset threshold, thermosensitivity, and capacity are improved compared to early stages of pregnancy.

Conclusion

This thesis illustrates that total body weight independent from pregnancy timepoint influences heat production during rest and exercise (i.e., shown in *Study 1 and 2*). Furthermore, the scoping review outcomes from *Study 3* suggest that, in various conditions, evaporative and dry heat loss mechanisms improve as pregnancy progresses. Therefore, future research should assess exercise at a fixed heat production with women of similar weight across pregnancy to measure outcomes of dry and evaporative heat loss mechanisms and, ultimately, core temperature responses.

CHAPTER 7: REFERENCES

ACOG committee opinion. Exercise during pregnancy and the postpartum period (2002). Number 267, January 2002. American College of Obstetricians and Gynecologists. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 77, 79-81.

Physical Activity and Exercise During Pregnancy and the Postpartum Period: ACOG Committee Opinion, Number 804 (2020). *Obstetrics and gynecology* 135, e178-e188.

Abramson DI, Flachs K & Fierst SM. (1943). Peripheral blood flow during gestation. *American Journal of Obstetrics & Gynecology* 45, 666-671.

Anim-Nyame N, Sooranna SR, Johnson MR, Gamble J & Steer PJ. (2000). Resting peripheral blood flow in normal pregnancy and in pre-eclampsia. *Clinical science (London, England : 1979)* 99, 505-510.

Arksey H & O'Malley L. (2005). Scoping studies: towards a methodological framework. *International journal of social research methodology* 8, 19-32.

Asakura H. (2004). Fetal and neonatal thermoregulation. *Journal of Nippon Medical School* 71, 360-370.

Baciuk EP, Pereira RI, Cecatti JG, Braga AF & Cavalcante SR. (2008). Water aerobics in pregnancy: Cardiovascular response, labor and neonatal outcomes. *Reproductive health* 5, 10.

Baker HJ, Lindsey JR & Weisbroth SH. (1979). Preface. In *The Laboratory Rat*, ed. Baker HJ, Lindsey JR & Weisbroth SH, pp. xi-xii. Academic Press.

Barrett L, Gaynor D, Rendall D, Mitchell D & Henzi SP. (2004). Habitual cave use and thermoregulation in chacma baboons (Papio hamadryas ursinus). *Journal of Human Evolution* 46, 215-222.

Basu R, Malig B & Ostro B. (2010). High ambient temperature and the risk of preterm delivery. *Am J Epidemiol* 172, 1108-1117.

Basu R, Rau R, Pearson D & Malig B. (2018). Temperature and Term Low Birth Weight in California. *American Journal of Epidemiology* 187, 2306-2314.

Beinder E, Huch A & Huch R. (1990). Peripheral skin temperature and microcirculatory reactivity during pregnancy. A study with thermography. *Journal of perinatal medicine* 18, 383-390.

Benzinger TH. (1969). Heat regulation: homeostasis of central temperature in man. *Physiol Rev* 49, 671-759.

Berglund LG & Gonzalez RR. (1977). Evaporation of sweat from sedentary man in humid environments. *Journal of applied physiology: respiratory, environmental and exercise physiology* 42, 767-772.

Bicca-Marques JC & Calegaro-Marques C. (1998). Behavioral thermoregulation in a sexually and developmentally dichromatic neotropical primate, the black-and-gold howling monkey (Alouatta caraya). *American journal of physical anthropology* 106, 533-546.

Bligh J. (2006). A theoretical consideration of the means whereby the mammalian core temperature is defended at a null zone. *J Appl Physiol* 100, 1332-1337.

Borg GA. (1982). Psychophysical bases of perceived exertion. *Medicine and science in sports and exercise* 14, 377-381.

Boulant JA & Bignall KE. (1973). Hypothalamic neuronal responses to peripheral and deep-body temperatures. *Am J Physiol* 225, 1371-1374.

Brearley AL, Sherburn M, Galea MP & Clarke SJ. (2015). Pregnant women maintain body temperatures within safe limits during moderate-intensity aqua-aerobic classes conducted in pools heated up to 33 degrees Celsius: an observational study. *Journal of physiotherapy* 61, 199-203.

Breithaupt P, Adamo KB & Colley RC. (2012). The HALO submaximal treadmill protocol to measure cardiorespiratory fitness in obese children and youth: a proof of principle study. *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme* 37, 308-314.

Brengelmann GL, Johnson JM, Hermansen L & Rowell LB. (1977). Altered control of skin blood flow during exercise at high internal temperatures. *J Appl Physiol* 43, 790-794.

Bronstein MN, Mak RP & King JC. (1995). The thermic effect of food in normal-weight and overweight pregnant women. *The British journal of nutrition* 74, 261-275.

Butte NF, Ellis KJ, Wong WW, Hopkinson JM & Smith EO. (2003). Composition of gestational weight gain impacts maternal fat retention and infant birth weight. *American journal of obstetrics and gynecology* 189, 1423-1432.

Butte NF, Hopkinson JM, Mehta N, Moon JK & Smith EO. (1999). Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation. *Am J Clin Nutr* 69, 299-307.

Butte NF, Wong WW, Treuth MS, Ellis KJ & O'Brian Smith E. (2004). Energy requirements during pregnancy based on total energy expenditure and energy deposition. *Am J Clin Nutr* 79, 1078-1087.

Byrne NM, Groves AM, McIntyre HD & Callaway LK. (2011). Changes in resting and walking energy expenditure and walking speed during pregnancy in obese women. *The American journal of clinical nutrition* 94, 819-830.

Campos FA & Fedigan LM. (2009). Behavioral adaptations to heat stress and water scarcity in white-faced capuchins (Cebus capucinus) in Santa Rosa National Park, Costa Rica. *American journal of physical anthropology* 138, 101-111.

Candas V, Libert JP & Vogt JJ. (1979a). Human skin wettedness and evaporative efficiency of sweating. *Journal of applied physiology: respiratory, environmental and exercise physiology* 46, 522-528.

Candas V, Libert JP & Vogt JJ. (1979b). Influence of air velocity and heat acclimation on human skin wettedness and sweating efficiency. *Journal of applied physiology: respiratory, environmental and exercise physiology* 47, 1194-1200.

Cankar K, Potocnik N & Strucl M. (2010). Alteration of skin laser-Doppler flux response to local cooling in gestational hypertension. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society* 20, 183-190.

Carbillon L, Uzan M & Uzan S. (2000). Pregnancy, vascular tone, and maternal hemodynamics: a crucial adaptation. *Obstet Gynecol Surv* 55, 574-581.

Carmichael S, Abrams B & Selvin S. (1997). The association of pattern of maternal weight gain with length of gestation and risk of spontaneous preterm delivery. *Paediatric and perinatal epidemiology* 11, 392-406.

Carpenter MW, Sady SP, Sady MA, Haydon B, Coustan DR & Thompson PD. (1990). Effect of maternal weight gain during pregnancy on exercise performance. *Journal of applied physiology (Bethesda, Md : 1985)* 68, 1173-1176.

Cena K & de Dear R. (2001). Thermal comfort and behavioural strategies in office buildings located in a hot-arid climate. *Journal of Thermal Biology* 26, 409-414.

Chandler KD & Bell AW. (1981). Effects of maternal exercise on fetal and maternal respiration and nutrient metabolism in the pregnant ewe. *Journal of developmental physiology* 3, 161-176.

Chapman AB, Abraham WT, Zamudio S, Coffin C, Merouani A, Young D, Johnson A, Osorio F, Goldberg C, Moore LG, Dahms T & Schrier RW. (1998). Temporal relationships between hormonal and hemodynamic changes in early human pregnancy. *Kidney international* 54, 2056-2063.

Chung JG, Taylor RS, Thompson JM, Anderson NH, Dekker GA, Kenny LC & McCowan LM. (2013). Gestational weight gain and adverse pregnancy outcomes in a nulliparous cohort. *European journal of obstetrics, gynecology, and reproductive biology* 167, 149-153.

Clapp JF. (2006). Influence of endurance exercise and diet on human placental development and fetal growth. *Placenta* 27, 527-534.

Clapp JF, 3rd. (1980). Acute exercise stress in the pregnant ewe. *American journal of obstetrics and gynecology* 136, 489-494.

Clapp JF, 3rd. (1991). The changing thermal response to endurance exercise during pregnancy. *American journal of obstetrics and gynecology* 165, 1684-1689.

Clapp JF, 3rd & Capeless E. (1997). Cardiovascular function before, during, and after the first and subsequent pregnancies. *The American journal of cardiology* 80, 1469-1473.

Clapp JF, 3rd, Stepanchak W, Tomaselli J, Kortan M & Faneslow S. (2000). Portal vein blood flow-effects of pregnancy, gravity, and exercise. *American journal of obstetrics and gynecology* 183, 167-172.

Clapp JF, 3rd, Wesley M & Sleamaker RH. (1987). Thermoregulatory and metabolic responses to jogging prior to and during pregnancy. *Medicine and science in sports and exercise* 19, 124-130.

Clarke PE & Gross H. (2004). Women's behaviour, beliefs and information sources about physical exercise in pregnancy. *Midwifery* 20, 133-141.

Clarke PE, Rousham EK, Gross H, Halligan AW & Bosio P. (2005). Activity patterns and time allocation during pregnancy: a longitudinal study of British women. *Annals of human biology* 32, 247-258.

Colley R, Connor Gorber S & Tremblay MS. (2010). Quality control and data reduction procedures for accelerometry-derived measures of physical activity. *Health reports* 21, 63-69.

Cotter JD, Patterson MJ & Taylor NA. (1995). The topography of eccrine sweating in humans during exercise. *Eur J Appl Physiol* 71, 549-554.

Cramer MN & Jay O. (2016). Biophysical aspects of human thermoregulation during heat stress. *Autonomic neuroscience : basic & clinical* 196, 3-13.

Cramp AG & Bray SR. (2009). A prospective examination of exercise and barrier self-efficacy to engage in leisure-time physical activity during pregnancy. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine* 37, 325-334.

Curet LB, Orr JA, Rankin HG & Ungerer T. (1976). Effect of exercise on cardiac output and distribution of uterine blood flow in pregnant ewes. *J Appl Physiol* 40, 725-728.

da Silva DF, Mohammad S, Hutchinson KA & Adamo KB. (2020). Cross-Validation of Ratings of Perceived Exertion Derived from Heart Rate Target Ranges Recommended for Pregnant Women. *International journal of exercise science* 13, 1340-1351.

Davenport MH, Ruchat SM, Mottola MF, Davies GA, Poitras VJ, Gray CE, Garcia AJ, Barrowman N, Adamo KB, Duggan M, Barakat R, Chilibeck P, Fleming K, Forte M, Korolnek J, Nagpal T, Slater LG, Stirling D & Zehr L. (2018a). 2019 Canadian Guideline for Physical Activity Throughout Pregnancy: Methodology. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC* 40, 1468-1483.

Davenport MH, Ruchat SM, Poitras VJ, Jaramillo Garcia A, Gray CE, Barrowman N, Skow RJ, Meah VL, Riske L, Sobierajski F, James M, Kathol AJ, Nuspl M, Marchand AA, Nagpal TS, Slater LG, Weeks A, Adamo KB, Davies GA, Barakat R & Mottola MF. (2018b). Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. *British journal of sports medicine* 52, 1367-1375.

Davenport MH, Ruchat SM, Sobierajski F, Poitras VJ, Gray CE, Yoo C, Skow RJ, Jaramillo Garcia A, Barrowman N, Meah VL, Nagpal TS, Riske L, James M, Nuspl M, Weeks A, Marchand AA, Slater LG, Adamo KB, Davies GA, Barakat R & Mottola MF. (2019a). Impact of prenatal exercise on maternal harms, labour and delivery outcomes: a systematic review and meta-analysis. *British journal of sports medicine* 53, 99-107.

Davenport MH, Sobierajski F, Mottola MF, Skow RJ, Meah VL, Poitras VJ, Gray CE, Jaramillo Garcia A, Barrowman N, Riske L, James M, Nagpal TS, Marchand AA, Slater LG, Adamo KB, Davies GA, Barakat R & Ruchat SM. (2018c). Glucose responses to acute and chronic exercise during pregnancy: a systematic review and meta-analysis. *Br J Sports Med* 52, 1357-1366.

Davenport MH, Yoo C, Mottola MF, Poitras VJ, Jaramillo Garcia A, Gray CE, Barrowman N, Davies GA, Kathol A, Skow RJ, Meah VL, Riske L, Sobierajski F, James M, Nagpal TS, Marchand AA, Slater LG, Adamo KB, Barakat R & Ruchat SM. (2019b). Effects of prenatal exercise on incidence of congenital anomalies and hyperthermia: a systematic review and meta-analysis. *British journal of sports medicine* 53, 116-123.

Davies GA, Maxwell C, McLeod L, Gagnon R, Basso M, Bos H, Delisle MF, Farine D, Hudon L, Menticoglou S, Mundle W, Murphy-Kaulbeck L, Ouellet A, Pressey T, Roggensack A, Leduc D, Ballerman C, Biringer A, Duperron L, Jones D, Lee LS, Shepherd D & Wilson K. (2010). SOGC Clinical Practice Guidelines: Obesity in pregnancy. No. 239, February 2010. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 110, 167-173.

Davies GA, Wolfe LA, Mottola MF & MacKinnon C. (2003a). Joint SOGC/CSEP clinical practice guideline: exercise in pregnancy and the postpartum period. *Canadian journal of applied physiology = Revue canadienne de physiologie appliquee* 28, 330-341.

Davies GA, Wolfe LA, Mottola MF, MacKinnon C, Arsenault MY, Bartellas E, Cargill Y, Gleason T, Iglesias S, Klein M, Martel MJ, Roggensack A, Wilson K, Gardiner P, Graham T, Haennel R, Hughson R, MacDougall D, McDermott J, Ross R, Tiidus P & Trudeau F. (2003b). Exercise in pregnancy and the postpartum period. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC* 25, 516-529.

Denize KM, Akbari P, da Silva DF, Haman F & Adamo KB. (2019). Greater energy demand of exercise during pregnancy does not impact mechanical efficiency. *Appl Physiol Nutr Metab*.

Deputy NP, Sharma AJ & Kim SY. (2015). Gestational Weight Gain - United States, 2012 and 2013. *MMWR Morbidity and mortality weekly report* 64, 1215-1220.

Dervis S, Coombs GB, Chaseling GK, Filingeri D, Smoljanic J & Jay O. (2016). A comparison of thermoregulatory responses to exercise between mass-matched groups with large differences in body fat. *Journal of applied physiology (Bethesda, Md : 1985)* 120, 615-623.

Desai DK, Moodley J & Naidoo DP. (2004). Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. *Obstetrics and gynecology* 104, 20-29.

Devlieger R, Benhalima K, Damm P, Van Assche A, Mathieu C, Mahmood T, Dunne F & Bogaerts A. (2016). Maternal obesity in Europe: where do we stand and how to move forward?: A scientific paper commissioned by the European Board and College of Obstetrics and Gynaecology (EBCOG). *European journal of obstetrics, gynecology, and reproductive biology* 201, 203-208.

DiNallo JM, Le Masurier GC, Williams NI & Downs DS. (2008). Walking for health in pregnancy: assessment by indirect calorimetry and accelerometry. *Research quarterly for exercise and sport* 79, 28-35.

Dobson KL, da Silva DF, Dervis S, Mohammad S, Nagpal TS & Adamo KB. (2020). Physical activity and gestational weight gain predict physiological and perceptual responses to exercise during pregnancy. *Birth defects research*.

Dodd JM, Turnbull D, McPhee AJ, Deussen AR, Grivell RM, Yelland LN, Crowther CA, Wittert G, Owens JA & Robinson JS. (2014). Antenatal lifestyle advice for women who are overweight or obese: LIMIT randomised trial. *BMJ (Clinical research ed)* 348, g1285.

Downey J. (2008). Perceptions and experiences of women who continue vigorous physical activity during pregnancy, pp. 124. Memorial University of Newfoundland (Canada), Ann Arbor.

Dubois D & Dubois E. (1916). A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med* 17, 863-871.

Duncan L & Pillay N. (2013). Shade as a thermoregulatory resource for captive chimpanzees. *Journal of Thermal Biology* 38, 169–177.

Dunlap SR. (2003). Thermoregulation in shallow water aquatic exercise during second trimester pregnancy, pp. 93. University of Idaho, Ann Arbor.

Edwards MJ. (1968). Congenital malformations in the rat following induced hyperthermia during gestation. *Teratology* 1, 173-177.

Edwards MJ. (1969). Congenital defects in guinea pigs: fetal resorptions, abortions, and malformations following induced hyperthermia during early gestation. *Teratology* 2, 313-328.

Edwards MJ, Saunders RD & Shiota K. (2003). Effects of heat on embryos and foetuses. *International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group* 19, 295-324.

Ejidokun OO. (2000). Community attitudes to pregnancy, anaemia, iron and folate supplementation in urban and rural Lagos, south-western Nigeria. *Midwifery* 16, 89-95.

El Bacha T, Luz M & Da Poian A. (2010). Dynamic adaptation of nutrient utilization in humans. *Nat Educ* 3.

Erkkola RU, Pirhonen JP & Kivijärvi AK. (1992). Flow velocity waveforms in uterine and umbilical arteries during submaximal bicycle exercise in normal pregnancy. *Obstetrics and gynecology* 79, 611-615.

Evenson KR, Barakat R, Brown WJ, Dargent-Molina P, Haruna M, Mikkelsen EM, Mottola MF, Owe KM, Rousham EK & Yeo S. (2014). Guidelines for Physical Activity during Pregnancy: Comparisons From Around the World. *Am J Lifestyle Med* 8, 102-121.

Evenson KR & Wen F. (2011). Prevalence and correlates of objectively measured physical activity and sedentary behavior among US pregnant women. *Preventive medicine* 53, 39-43.

Fawer R, Dettling A, Weihs D, Welti H & Schelling JL. (1978). Effect of the menstrual cycle, oral contraception and pregnancy on forearm blood flow, venous distensibility and clotting factors. *European journal of clinical pharmacology* 13, 251-257.

Ferraro ZM, Barrowman N, Prud'homme D, Walker M, Wen SW, Rodger M & Adamo KB. (2012a). Excessive gestational weight gain predicts large for gestational age neonates independent of maternal body mass index. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet* 25, 538-542.

Ferraro ZM, Contador F, Tawfiq A, Adamo KB & Gaudet L. (2015). Gestational weight gain and medical outcomes of pregnancy. *Obstetric medicine* 8, 133-137.

Ferraro ZM, Gaudet L & Adamo KB. (2012b). The potential impact of physical activity during pregnancy on maternal and neonatal outcomes. *Obstetrical & gynecological survey* 67, 99-110.

Forsum E, Kabir N, Sadurskis A & Westerterp K. (1992). Total energy expenditure of healthy Swedish women during pregnancy and lactation. *The American journal of clinical nutrition* 56, 334-342.

Franklin A, Mishtal J, Johnson T & Simms-Cendan J. (2017a). Rowers' Self-Reported Behaviors, Attitudes, and Safety Concerns Related to Exercise, Training, and Competition During Pregnancy. *Cureus* 9, e1534.

Franklin A, Mishtal J, Johnson T & Simms-Cendan J. (2017b). Rowers' Self-Reported Behaviors, Attitudes, and Safety Concerns Related to Exercise, Training, and Competition During Pregnancy. *Cureus* 9, e1534-e1534.

Fusco MM, Hardy JD & Hammel HT. (1961). Interaction of central and peripheral factors in physiological temperature regulation. *Am J Physiol* 200, 572-580.

Gagge AP & Gonzales RR. (1996). Mechanisms of heat exchange In *Handbook of Physiology Section 4: Environmental Physiology*, ed. Fregley MJ & Blatteis CM, pp. 45-84. Oxford University press, New York, NY.

Gagge AP, Stolwijk JA & Saltin B. (1969). Comfort and thermal sensations and associated physiological responses during exercise at various ambient temperatures. *Environ Res* 2, 209-229.

Gagnon D & Kenny GP. (2012). Sex differences in thermoeffector responses during exercise at fixed requirements for heat loss. *J Appl Physiol (1985)* 113, 746-757.

Gaston A & Vamos CA. (2013). Leisure-time physical activity patterns and correlates among pregnant women in Ontario, Canada. *Maternal and child health journal* 17, 477-484.

Gilmore LA, Butte NF, Ravussin E, Han H, Burton JH & Redman LM. (2016). Energy Intake and Energy Expenditure for Determining Excess Weight Gain in Pregnant Women. *Obstetrics and gynecology* 127, 884-892.

Ginsburg J & Duncan SL. (1967). Peripheral circulation in hypertensive pregnancy. *Cardiovascular research* 1, 356-361.

Goldberg GR, Prentice AM, Coward WA, Davies HL, Murgatroyd PR, Wensing C, Black AE, Harding M & Sawyer M. (1993). Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. *The American journal of clinical nutrition* 57, 494-505.

Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH, Li N, Hu G, Corrado F, Rode L, Kim YJ, Haugen M, Song WO, Kim MH, Bogaerts A, Devlieger R, Chung JH & Teede HJ. (2017). Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis. *Jama* 317, 2207-2225.

Graham JM, Jr., Edwards MJ & Edwards MJ. (1998). Teratogen update: gestational effects of maternal hyperthermia due to febrile illnesses and resultant patterns of defects in humans. *Teratology* 58, 209-221.

Guelfi KJ, Wang C, Dimmock JA, Jackson B, Newnham JP & Yang H. (2015). A comparison of beliefs about exercise during pregnancy between Chinese and Australian pregnant women. *BMC pregnancy and childbirth* 15, 345.

Hammel HT. (1968). Regulation of internal body temperature. *Ann Rev Physiol* 30, 641-710.

Hammel HT, Hardy JD & Fusco MM. (1960). Thermoregulatory responses to hypothalamic cooling in unanesthetized dogs. *Am J Physiol* 198, 481-486.

Hankenson FC, Marx JO, Gordon CJ & David JM. (2018). Effects of Rodent Thermoregulation on Animal Models in the Research Environment. *Comp Med* 68, 425-438.

Hartgill TW, Bergersen TK & Pirhonen J. (2011). Core body temperature and the thermoneutral zone: a longitudinal study of normal human pregnancy. *Acta physiologica (Oxford, England)* 201, 467-474.

Hartmann S & Bung P. (1999). Physical exercise during pregnancy--physiological considerations and recommendations. *Journal of perinatal medicine* 27, 204-215.

Havenith G. (2001). Human surface to mass ratio and body core temperature in exercise heat stress - a concept revisited. *J Therm Biol* 26, 387-393.

Havenith G. (2005). Temperature Regulation, Heat Balance and Climatic Stress. In *Extreme Weather Events and Public Health Responses*, ed. Kirch W, Bertollini R & Menne B, pp. 69-80. Springer Berlin Heidelberg, Berlin, Heidelberg.

Havenith G, Coenen JM, Kistemaker L & Kenney WL. (1998). Relevance of individual characteristics for human heat stress response is dependent on exercise intensity and climate type. *European journal of applied physiology and occupational physiology* 77, 231-241.

Havenith G & van Middendorp H. (1990). The relative influence of physical fitness, acclimatization state, anthropometric measures and gender on individual reactions to heat stress. *Eur J Appl Physiol* 61, 419-427.

Hegewald MJ & Crapo RO. (2011). Respiratory physiology in pregnancy. *Clinics in chest medicine* 32, 1-13.

Heini A, Schutz Y, Diaz E, Prentice AM, Whitehead RG & Jéquier E. (1991). Free-living energy expenditure measured by two independent techniques in pregnant and nonpregnant Gambian women. *The American journal of physiology* 261, E9-17.

Huang TW & Kuo AD. (2014). Mechanics and energetics of load carriage during human walking. *The Journal of experimental biology* 217, 605-613.

Hytten FE & Leitch I. (1971). *The physiology of human pregnancy*. Blackwell, London.

I.O.M & National Research Council Committee to Reexamine Pregnancy Weight Guidelines IoM. (2009). The National Academies Collection: Reports funded by National Institutes of Health. *Weight Gain During Pregnancy: Reexamining the Guidelines*.

Iacobaeus C, Andolf E, Thorsell M, Bremme K, Jörneskog G, Östlund E & Kahan T. (2017). Longitudinal study of vascular structure and function during normal pregnancy. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology* 49, 46-53.

Inoue Y, Tanaka Y, Omori K, Kuwahara T, Ogura Y & Ueda H. (2005). Sex- and menstrual cycle-related differences in sweating and cutaneous blood flow in response to passive heat exposure. *Eur J Appl Physiol* 94, 323-332.

Jacquot CM, Schellen L, Kingma BR, van Baak MA & van Marken Lichtenbelt WD. (2014). Influence of thermophysiology on thermal behavior: the essentials of categorization. *Physiol Behav* 128, 180-187.

Jeffreys RM, Stepanchak W, Lopez B, Hardis J & Clapp JF, 3rd. (2006). Uterine blood flow during supine rest and exercise after 28 weeks of gestation. *BJOG : an international journal of obstetrics and gynaecology* 113, 1239-1247.

Jessen C. (1996). Interaction of body temperatures in control of thermoregulatory effector mechanisms. In *Handbook of physiology Section 4: Environmental physiology*, ed. Fregly MJ & Blatteis CM, pp. 127-138. Oxford University press New York, NY.

Johnson J, Clifton RG, Roberts JM, Myatt L, Hauth JC, Spong CY, Varner MW, Wapner RJ, Thorp JM, Jr., Mercer BM, Peaceman AM, Ramin SM, Samuels P, Sciscione A, Harper M, Tolosa JE, Saade G & Sorokin Y. (2013a). Pregnancy outcomes with weight gain above or below the 2009 Institute of Medicine guidelines. *Obstetrics and gynecology* 121, 969-975.

Jones RL, Botti JJ, Anderson WM & Bennett NL. (1985). Thermoregulation during aerobic exercise in pregnancy. *Obstetrics and gynecology* 65, 340-345.

Karjalainen S. (2012). Thermal comfort and gender: a literature review. *Indoor air* 22, 96-109.

Katz VL. (1996). Water exercise in pregnancy. *Seminars in perinatology* 20, 285-291.

Kenny GP, Stapleton JM, Yardley JE, Boulay P & Sigal RJ. (2013). Older adults with type 2 diabetes store more heat during exercise. *Med Sci Sports Exerc* 45, 1906-1914.

Kenny GP, Yardley J, Brown C, Sigal RJ & Jay O. (2010). Heat stress in older individuals and patients with common chronic diseases. *CMAJ* 182, 1053-1060.

Kingma B, Frijns A & van Marken Lichtenbelt W. (2012). The thermoneutral zone: Implications for metabolic studies. *Frontiers in bioscience (Elite edition)* 4, 1975-1985.

Knuttgen HG & Emerson K, Jr. (1974). Physiological response to pregnancy at rest and during exercise. *J Appl Physiol* 36, 549-553.

Kondo N, Takano S, Aoki K, Shibasaki M, Tominaga H & Inoue Y. (1998). Regional differences in the effect of exercise intensity on thermoregulatory sweating and cutaneous vasodilation. *Acta Physiol Scand* 164, 71-78.

Kopp-Hoolihan LE, van Loan MD, Wong WW & King JC. (1999). Longitudinal assessment of energy balance in well-nourished, pregnant women. *The American journal of clinical nutrition* 69, 697-704.

Kukkonen-Harjula K & Kauppinen K. (2006). Health effects and risks of sauna bathing. *International journal of circumpolar health* 65, 195-205.

Lamarche DT, Notley SR, Louie JC, Poirier MP & Kenny GP. (2018). Fitness-related differences in the rate of whole-body evaporative heat loss in exercising men are heat-load dependent. *Exp Physiol* 103, 101-110.

Langford A, Joshu C, Chang JJ, Myles T & Leet T. (2011). Does gestational weight gain affect the risk of adverse maternal and infant outcomes in overweight women? *Maternal and child health journal* 15, 860-865.

Larsson L & Lindqvist PG. (2005). Low-impact exercise during pregnancy--a study of safety. *Acta obstetricia et gynecologica Scandinavica* 84, 34-38.

Lederman SA, Paxton A, Heymsfield SB, Wang J, Thornton J & Pierson RN, Jr. (1997). Body fat and water changes during pregnancy in women with different body weight and weight gain. *Obstetrics and gynecology* 90, 483-488.

Lemmens PMC, Sartor F, Cox LGE, den Boer SV & Westerink J. (2018). Evaluation of an activity monitor for use in pregnancy to help reduce excessive gestational weight gain. *BMC pregnancy and childbirth* 18, 312.

Lindqvist PG, Marsal K, Merlo J & Pirhonen JP. (2003). Thermal response to submaximal exercise before, during and after pregnancy: a longitudinal study. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet* 13, 152-156.

Lof M & Forsum E. (2006). Activity pattern and energy expenditure due to physical activity before and during pregnancy in healthy Swedish women. *The British journal of nutrition* 95, 296-302.

Lof M, Olausson H, Bostrom K, Janerot-Sjöberg B, Sohlstrom A & Forsum E. (2005). Changes in basal metabolic rate during pregnancy in relation to changes in body weight and composition, cardiac output, insulin-like growth factor I, and thyroid hormones and in relation to fetal growth. *The American journal of clinical nutrition* 81, 678-685.

Lotgering FK, Gilbert RD & Longo LD. (1983). Exercise responses in pregnant sheep: blood gases, temperatures, and fetal cardiovascular system. *J Appl Physiol Respir Environ Exerc Physiol* 55, 842-850.

Macaulay JH, Randall NR, Bond K & Steer PJ. (1992). Continuous monitoring of fetal temperature by noninvasive probe and its relationship to maternal temperature, fetal heart rate, and cord arterial oxygen and pH. *Obstetrics and gynecology* 79, 469-474.

Majolo B, McFarland R, Young C & Qarro M. (2013). The Effect of Climatic Factors on the Activity Budgets of Barbary Macaques. *International Journal of Primatology* 34, 500-514.

Marks LE & Gonzalez RR. (1974). Skin temperature modifies the pleasantness of thermal stimuli. *Nature* 247, 473-475.

McFarland R, Barrett L, Costello MA, Fuller A, Hetem RS, Maloney SK, Mitchell D & Henzi PS. (2019). Keeping cool in the heat: Behavioral thermoregulation and body temperature patterns in wild vervet monkeys. *Am J Phys Anthropol*.

McMurray RG, Berry MJ, Katz VL, Graetzer DG & Cefalo RC. (1990). The thermoregulation of pregnant women during aerobic exercise in the water: a longitudinal approach. *Eur J Appl Physiol Occup Physiol* 61, 119-123.

McMurray RG & Katz VL. (1990). Thermoregulation in pregnancy. Implications for exercise. *Sports medicine (Auckland, NZ)* 10, 146-158.

McMurray RG, Katz VL, Meyer-Goodwin WE & Cefalo RC. (1993). Thermoregulation of pregnant women during aerobic exercise on land and in the water. *American journal of perinatology* 10, 178-182.

Medek H, Halldorsson T, Gunnarsdottir I & Geirsson RT. (2016). Physical activity of relatively high intensity in mid-pregnancy predicts lower glucose tolerance levels. *Acta obstetricia et gynecologica Scandinavica* 95, 1055-1062.

Melzer K, Schutz Y, Boulvain M & Kayser B. (2009). Pregnancy-related changes in activity energy expenditure and resting metabolic rate in Switzerland. *Eur J Clin Nutr* 63, 1185-1191.

Melzer K, Schutz Y, Soehnchen N, Othenin Girard V, Martinez de Tejada B, Pichard C, Irion O, Boulvain M & Kayser B. (2010). Prepregnancy body mass index and resting metabolic rate during pregnancy. *Annals of nutrition & metabolism* 57, 221-227.

Metcalfe J & Ueland K. (1974). Maternal cardiovascular adjustments to pregnancy. *Prog Cardiovasc Dis* 16, 363-374.

Miller MW, Nyborg WL, Dewey WC, Edwards MJ, Abramowicz JS & Brayman AA. (2002). Hyperthermic teratogenicity, thermal dose and diagnostic ultrasound during pregnancy: implications of new standards on tissue heating. *International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group* 18, 361-384.

Mitchell D, Snelling EP, Hetem RS, Maloney SK, Strauss WM & Fuller A. (2018). Revisiting concepts of thermal physiology: Predicting responses of mammals to climate change. *J Anim Ecol* 87, 956-973.

Moore DH, Jarrett JC, 2nd & Bendick PJ. (1988). Exercise-induced changes in uterine artery blood flow, as measured by Doppler ultrasound, in pregnant subjects. *American journal of perinatology* 5, 94-97.

Morris SN & Johnson NR. (2005). Exercise during pregnancy: a critical appraisal of the literature. *The Journal of reproductive medicine* 50, 181-188.

Most J, Amant MS, Hsia DS, Altazan AD, Thomas DM, Gilmore LA, Vallo PM, Beyl RA, Ravussin E & Redman LM. (2019a). Evidence-based recommendations for energy intake in pregnant women with obesity. *J Clin Invest* 129, 4682-4690.

Most J, Dervis S, Haman F, Adamo KB & Redman LM. (2019b). Energy Intake Requirements in Pregnancy. *Nutrients* 11, 1812.

Most J, Marlatt KL, Altazan AD & Redman LM. (2018). Advances in assessing body composition during pregnancy. *Eur J Clin Nutr* 72, 645-656.

Mottola MF, Davenport MH, Brun CR, Inglis SD, Charlesworth S & Sopper MM. (2006). VO2peak prediction and exercise prescription for pregnant women. *Medicine and science in sports and exercise* 38, 1389-1395.

Mottola MF, Davenport MH, Ruchat S-M, Davies GA, Poitras VJ, Gray CE, Jaramillo Garcia A, Barrowman N, Adamo KB, Duggan M, Barakat R, Chilibeck P, Fleming K, Forte M, Korolnek J, Nagpal T, Slater LG, Stirling D & Zehr L. (2018a). 2019 Canadian guideline for physical activity throughout pregnancy. *British journal of sports medicine* 52, 1339.

Moya J, Phillips L, Sanford J, Wooton M, Gregg A & Schuda L. (2014). A review of physiological and behavioral changes during pregnancy and lactation: potential exposure factors and data gaps. *Journal of exposure science & environmental epidemiology* 24, 449-458.

Myhrman P, Jansson I & Lundgren Y. (1980). Skin blood flow in normal pregnancy measured by venous occlusion plethysmography of the hand. *Acta obstetricia et gynecologica Scandinavica* 59, 107-110.

Nadel ER, Mitchell JW, Saltin B & Stolwijk JA. (1971). Peripheral modifications to the central drive for sweating. *J Appl Physiol* 31, 828-833.

Nadel ER, Pandolf KB, Roberts MF & Stolwijk JA. (1974). Mechanisms of thermal acclimation to exercise and heat. *J Appl Physiol* 37, 515-520.

Nagashima K. (2006). Central mechanisms for thermoregulation in a hot environment. *Ind Health* 44, 359-367.

Nakamura M, Yoda T, Crawshaw LI, Yasuhara S, Saito Y, Kasuga M, Nagashima K & Kanosue K. (2008). Regional differences in temperature sensation and thermal comfort in humans. *J Appl Physiol (1985)* 105, 1897-1906.

Nascimento SL, Surita FG & Cecatti JG. (2012). Physical exercise during pregnancy: a systematic review. *Current opinion in obstetrics & gynecology* 24, 387-394.

Newton ER & May L. (2017). Adaptation of Maternal-Fetal Physiology to Exercise in Pregnancy: The Basis of Guidelines for Physical Activity in Pregnancy. *Clin Med Insights Womens Health* 10, 1179562X17693224-11179562X17693224.

Ngongalah L, Rankin J, Rapley T, Odeniyi A, Akhter Z & Heslehurst N. (2018). Dietary and physical activity behaviours in African migrant women living in high income countries: A systematic review and framework synthesis. *Nutrients* 10.

Nielsen B & Davies CT. (1976). Temperature regulation during exercise in water and air. *Acta physiologica Scandinavica* 98, 500-508.

Nishi Y. (1981). Measurement of thermal balance in man. *In: Bioengineering, thermal physiology and comfort, edited by Cena K and Clark J New York, NY: Elsevier,* , pp. 29-39.

Notley SR, Park J, Tagami K, Ohnishi N & Taylor NAS. (2017). Variations in body morphology explain sex differences in thermoeffector function during compensable heat stress. *Exp Physiol* 102, 545-562.

O'Neill ME. (1996). Maternal rectal temperature and fetal heart rate responses to upright cycling in late pregnancy. *British journal of sports medicine* 30, 32-35.

Ohlmann P, Jung F, Mrowietz C, Alt T, Alt S & Schmidt W. (2001). Peripheral microcirculation during pregnancy and in women with pregnancy induced hypertension. *Clinical hemorheology and microcirculation* 24, 183-191.

Parsons K. (2003). *Human thermal environments, the effect of hot, moderate and cold environments on human health, comfort and performance.* . CRC Press; 3 edition (April 9, 2014).

Passmore R & Durnin JV. (1955). Human energy expenditure. *Physiological reviews* 35, 801-840.

Pellerin N & Candas V. (2003). Combined effects of temperature and noise on human discomfort. *Physiology & Behavior* 78, 99-106.

Pernoll ML, Metcalfe J, Schlenker TL, Welch JE & Matsumoto JA. (1975). Oxygen consumption at rest and during exercise in pregnancy. *Respiration physiology* 25, 285-293.

Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, McInerney P, Godfrey CM & Khalil H. (2020). Updated methodological guidance for the conduct of scoping reviews. *JBI Evidence Synthesis* 18, 2119-2126.

Petraglia F, Woodruff TK, Botticelli G, Botticelli A, Genazzani AR, Mayo KE & Vale W. (1992). Gonadotropin-releasing hormone, inhibin, and activin in human placenta: evidence for a common cellular localization. *The Journal of clinical endocrinology and metabolism* 74, 1184-1188.

Petrella E, Malavolti M, Bertarini V, Pignatti L, Neri I, Battistini NC & Facchinetti F. (2014). Gestational weight gain in overweight and obese women enrolled in a healthy lifestyle and eating habits program. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet* 27, 1348-1352.

Petrov Fieril K, Glantz A & Fagevik Olsen M. (2016a). Hemodynamic responses to single sessions of aerobic exercise and resistance exercise in pregnancy. *Acta obstetricia et gynecologica Scandinavica* 95, 1042-1047.

Pierau F. (1996). Peripheral thermosensors. In *Handbook of physiology Section 4: Environmental physiology*, ed. Fregly M & Blatteis C, pp. 85-104. Oxford University press, New York, NY.

Piers LS, Diggavi SN, Thangam S, van Raaij JM, Shetty PS & Hautvast JG. (1995). Changes in energy expenditure, anthropometry, and energy intake during the course of pregnancy and lactation in well-nourished Indian women. *The American journal of clinical nutrition* 61, 501-513.

Pitkin RM. (1976). Nutritional support in obstetrics and gynecology. *Clinical obstetrics and gynecology* 19, 489-513.

Pivarnik JM. (1994). Maternal exercise during pregnancy. *Sports medicine (Auckland, NZ)* 18, 215-217.

Pivarnik JM, Lee W, Clark SL, Cotton DB, Spillman HT & Miller JF. (1990). Cardiac output responses of primigravid women during exercise determined by the direct Fick technique. *Obstetrics and gynecology* 75, 954-959.

Pivarnik JM, Lee W & Miller JF. (1991). Physiological and perceptual responses to cycle and treadmill exercise during pregnancy. *Medicine and science in sports and exercise* 23, 470-475.

Pivarnik JM, Marichal CJ, Spillman T & Morrow JRJr. (1992). Menstrual cycle phase affects temperature regulation during endurance exercise. *J Appl Physiol* 72, 543-548.

Poston L, Bell R, Croker H, Flynn AC, Godfrey KM, Goff L, Hayes L, Khazaezadeh N, Nelson SM, Oteng-Ntim E, Pasupathy D, Patel N, Robson SC, Sandall J, Sanders TA, Sattar N, Seed PT, Wardle J, Whitworth MK & Briley AL. (2015). Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): a multicentre, randomised controlled trial. *The lancet Diabetes & endocrinology* 3, 767-777.

Power GG. (1989). Biology of temperature: the mammalian fetus. *Journal of developmental physiology* 12, 295-304.

Prentice AM, Goldberg GR, Davies HL, Murgatroyd PR & Scott W. (1989). Energy-sparing adaptations in human pregnancy assessed by whole-body calorimetry. *The British journal of nutrition* 62, 5-22.

Prentice AM, Poppitt SD, Goldberg GR & Prentice A. (1995). Adaptive strategies regulating energy balance in human pregnancy. *Human reproduction update* 1, 149-161.

Prentice AM, Spaaij CJ, Goldberg GR, Poppitt SD, van Raaij JM, Totton M, Swann D & Black AE. (1996). Energy requirements of pregnant and lactating women. *Eur J Clin Nutr* 50 Suppl 1, S82-110; discussion S110-111.

Prozesky OPM. (1963). Body Temperature of Birds in Relation to Nesting Habits. *Nature* 197, 401-402.

Purdy GM, James MA, Wakefield PK, Skow RJ, Van Diepen S, May LE, Davenport MH & Steinback CD. (2019). Maternal cardioautonomic responses during and following exercise throughout pregnancy. *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme* 44, 263-270.

Randall WC & Kimura KK. (1955). The pharmacology of sweating. *Pharmacol Rev* 7, 365-397.

Rasmussen KM, Catalano PM & Yaktine AL. (2009). New guidelines for weight gain during pregnancy: what obstetrician/gynecologists should know. *Current opinion in obstetrics & gynecology* 21, 521-526.

Ravanelli N, Casasola W, English T, Edwards KM & Jay O. (2019). Heat stress and fetal risk. Environmental limits for exercise and passive heat stress during pregnancy: a systematic review with best evidence synthesis. *British journal of sports medicine* 53, 799-805.

Robertshaw D. (2006). Mechanisms for the control of respiratory evaporative heat loss in panting animals. *Journal of Applied Physiology* 101, 664-668.

Romanovsky AA. (2007). Thermoregulation: some concepts have changed. Functional architecture of the thermoregulatory system. *Am J Physiol Regul Integr Comp Physiol* 292, R37-46.

Rousham EK, Clarke PE & Gross H. (2006). Significant changes in physical activity among pregnant women in the UK as assessed by accelerometry and self-reported activity. *Eur J Clin Nutr* 60, 393-400.

Ruchat SM, Mottola MF, Skow RJ, Nagpal TS, Meah VL, James M, Riske L, Sobierajski F, Kathol AJ, Marchand AA, Nuspl M, Weeks A, Gray CE, Poitras VJ, Jaramillo Garcia A, Barrowman N, Slater LG, Adamo KB, Davies GA, Barakat R & Davenport MH. (2018). Effectiveness of exercise interventions in the prevention of excessive gestational weight gain and postpartum weight retention: a systematic review and meta-analysis. *British journal of sports medicine* 52, 1347-1356.

Salvesen K, Hem E & Sundgot-Borgen J. (2012). Fetal wellbeing may be compromised during strenuous exercise among pregnant elite athletes. *British journal of sports medicine* 46, 279-283.

San-Frutos L, Engels V, Zapardiel I, Perez-Medina T, Almagro-Martinez J, Fernandez R & Bajo-Arenas JM. (2011). Hemodynamic changes during pregnancy and postpartum: a prospective study using thoracic electrical bioimpedance. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet* 24, 1333-1340.

Santo EC, Forbes PW, Oken E & Belfort MB. (2017). Determinants of physical activity frequency and provider advice during pregnancy. *BMC pregnancy and childbirth* 17, 286.

Sato K. (1977). The physiology, phramacology and biochemistry of the eccrine sweat gland. *Rev Physiol Biochem Phramacol* 79, 52-131.

Sato K. (1993). The mechanisms of eccrine sweat production. In *Perspectives in exercise science and sports medicine Volume 6: Exercise, heat , and thermoregulation*, ed. Gisofi CV, Lamb DR & Nadel ER, pp. 85-118. WCB Brown and Benchmark, Dubuque, IA.

Sato K & Dobson RL. (1970). Regional and individual variations in the function of the human eccrine sweat gland. *J Invest Dermatol* 54, 443-449.

Sato K, Kang WH, Saga K & Sato KT. (1989). Biology of sweat glands and their disorders. I. Normal sweat gland function. *J Am Acad Dermatol* 20, 537-563.

Sawka MN, Wenger CB & Pandolf KB. (1996). Thermoregulatory responses to acute exercise-heat stress and heat acclimation. In *Handbook of physiology Section 4: Environmental physiology*, ed. Fregly MJ & Blatteis CM, pp. 157-186. Oxford University press, New York, NY.

Schellen L, Loomans MGLC, de Wit MH, Olesen BW & Lichtenbelt WDvM. (2012). The influence of local effects on thermal sensation under non-uniform environmental conditions — Gender differences in thermophysiology, thermal comfort and productivity during convective and radiant cooling. *Physiology & Behavior* 107, 252-261.

Schlader ZJ, Perry BG, Jusoh MRC, Hodges LD, Stannard SR & Mündel T. (2013). Human temperature regulation when given the opportunity to behave. *European Journal of Applied Physiology* 113, 1291-1301.

Schlader ZJ, Simmons SE, Stannard SR & Mundel T. (2011). The independent roles of temperature and thermal perception in the control of human thermoregulatory behavior. *Physiol Behav* 103, 217-224.

Schröder HJ & Power GG. (1994). Increase of fetal arterial blood temperature by reduction of umbilical blood flow in chronically instrumented fetal sheep. *Pflugers Archiv : European journal of physiology* 427, 190-192.

Schröder HJ & Power GG. (1997). Engine and radiator: fetal and placental interactions for heat dissipation. *Experimental physiology* 82, 403-414.

Shibasaki M, Wilson TE & Crandall CG. (2006). Neural control and mechanisms of eccrine sweating during heat stress and exercise. *J Appl Physiol (1985)* 100, 1692-1701.

Sillero-Quintana M, Conde-Pascual E, Gomez-Carmona PM, Fernandez-Cuevas I & Garcia-Pastor T. (2012). Effect of Yoga and Swimming on body temperature of pregnant women. *Thermology International* 22, 143-149.

Simoes R, Vardasca R & Nogueira-Silva C. (2012). Thermal skin reference values in healthy late pregnancy. *Journal of Thermal Biology* 37, 608-614.

Song G-S, Lim J-H & Ahn T-K. (2012). Air conditioner operation behaviour based on students' skin temperature in a classroom. *Applied Ergonomics* 43, 211-216.

Soultanakis-Aligianni HN. (2003). Thermoregulation during exercise in pregnancy. *Clinical obstetrics and gynecology* 46, 442-455.

Soultanakis HN. (2016). Aquatic Exercise and Thermoregulation in Pregnancy. *Clinical obstetrics and gynecology* 59, 576-590.

Spaaij CJ, van Raaij JM, Van der Heijden LJ, Schouten FJ, Drijvers JJ, De Groot LC, Boekholt HA & Hautvast JG. (1994). No substantial reduction of the thermic effect of a meal during pregnancy in well-nourished Dutch women. *The British journal of nutrition* 71, 335-344.

Sparti A, DeLany JP, de la Bretonne JA, Sander GE & Bray GA. (1997). Relationship between resting metabolic rate and the composition of the fat-free mass. *Metabolism* 46, 1225-1230.

Spatling L, Fallenstein F, Huch A, Huch R & Rooth G. (1992). The variability of cardiopulmonary adaptation to pregnancy at rest and during exercise. *British journal of obstetrics and gynaecology* 99 Suppl 8, 1-40.

Stapleton JM, Poirier MP, Flouris AD, Boulay P, Sigal RJ, Malcolm J & Kenny GP. (2015a). Aging impairs heat loss, but when does it matter? *J Appl Physiol (1985)* 118, 299-309.

Stapleton JM, Poirier MP, Flouris AD, Boulay P, Sigal RJ, Malcolm J & Kenny GP. (2015b). At what level of heat load are age-related impairments in the ability to dissipate heat evident in females? *PLoS One* 10, e0119079.

Stark MJ, Dierkx L, Clifton VL & Wright IMR. (2006). Alterations in the Maternal Peripheral Microvascular Response in Pregnancies Complicated by Preeclampsia and the Impact of Fetal Sex. *Journal of the Society for Gynecologic Investigation* 13, 573-578.

Stelzner JK & Hausfater G. (1986). Posture, microclimate, and thermoregulation in yellow baboons. *Primates* 27, 449-463.

Stolwijk JAJ & Hardy JD. (2011). Control of Body Temperature. *Comprehensive Physiology*, 45-68.

Szymanski LM & Kogutt BK. (2018). Uterine Artery Doppler Velocimetry During Individually Prescribed Exercise in Pregnancy. *Obstetrics and gynecology* 132, 1026-1032.

Takano S, Kondo N, Shibasaki S, Aoki K, Inoue Y & Iwata A. (1996). The influence of work loads on regional differences in sweating rates. *Jpn J Physiol* 46, 183-186.

Tan EK & Tan EL. (2013). Alterations in physiology and anatomy during pregnancy. *Best practice & research Clinical obstetrics & gynaecology* 27, 791-802.

Thornburg KL, Jacobson SL, Giraud GD & Morton MJ. (2000). Hemodynamic changes in pregnancy. *Seminars in perinatology* 24, 11-14.

Tuffnell D, Buchan P, Albert D & Tyndale-biscoe S. (2009). Fetal heart rate responses to maternal exercise, increased maternal temperature and maternal circadian variation. *Journal of Obstetrics & Gynaecology* 10, 387-391.

Tuffnell DJ, Buchan PC, Albert D & Tyndale-biscoe S. (1990). Fetal heart rate responses to maternal exercise, increased maternal temperature and maternal circadian variation. *Journal of Obstetrics and Gynaecology* 10, 387-391.

Tur E, Tamir A & Guy RH. (1992a). Cutaneous blood flow in gestational hypertension and normal pregnancy. *The Journal of investigative dermatology* 99, 310-314.

Tur E, Tamir A & Guy RH. (1992b). Cutaneous blood flow in gestational hypertension and normal pregnancy. *Journal of Investigative Dermatology* 99, 310-314.

Vaha-Eskeli K, Erkkola R & Seppanen A. (1991). Is the heat dissipating ability enhanced during pregnancy? *European journal of obstetrics, gynecology, and reproductive biology* 39, 169-174.

Vähä-Eskeli K, Erkkola R & Seppänen A. (1991a). Is the heat dissipating ability enhanced during pregnancy? *European journal of obstetrics, gynecology, and reproductive biology* 39, 169-174.

Vähä-Eskeli KK, Erkkola RU, Seppänen A, Poranen AK & Säteri U. (1991b). Haemodynamic response to moderate thermal stress in pregnancy. *Annals of medicine* 23, 121-126.

Wang D, Zhang H, Arens E & Huizenga C. (2007). Observations of upper-extremity skin temperature and corresponding overall-body thermal sensations and comfort. *Building and Environment* 42, 3933-3943.

Weiner JS. (1945). The regional distribution of sweating. *J Physiol* 104, 32-40.

Wenger CB. (1972). Heat of evaporation of sweat: thermodynamic considerations. *J Appl Physiol* 32, 456-459.

Widen EM & Gallagher D. (2014). Body composition changes in pregnancy: measurement, predictors and outcomes. *European Journal of Clinical Nutrition* 68, 643-652.

Wissler EH. (2008). A quantitative assesment of skin blood flow in humans. *Eur J Appl Physiol* 104, 145-157.

Wolfe LA & Weissgerber TL. (2003). Clinical physiology of exercise in pregnancy: a literature review. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC* 25, 473-483.

Wulandari LP & Klinken Whelan A. (2011). Beliefs, attitudes and behaviours of pregnant women in Bali. *Midwifery* 27, 867-871.

Wyndham CH & Atkins AR. (1968). A physiological scheme and mathematical model of temperature regulation in man. *Pflugers Archiv : European journal of physiology* 303, 14-30.

Wyss CR, Brengelmann GL, Johnson JM, Rowell LB & Niederberger M. (1974). Control of skin blood flow, sweating, and heart rate: role of skin vs. core temperature. *J Appl Physiol* 36, 726-733.

Zhang H, Arens E, Huizenga C & Han T. (2010). Thermal sensation and comfort models for non-uniform and transient environments, part II: Local comfort of individual body parts. *Building and Environment - BLDG ENVIRON* 45, 389-398.

Ziskin MC & Morrissey J. (2011). Thermal thresholds for teratogenicity, reproduction, and development. *International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group* 27, 374-387.

CHAPTER 8: APPENDICES

APPENDIX I: INFORMED CONSENT FORM (PLACENTA)

PARTICIPANT INFORMED CONSENT FORM

Title of Study: Physica**L AC**tivity and di**E**tary implicatio**N**s **T**hroughout pregn**A**ncy **(PLACENTA)**

Investigators:

Kristi Adamo, Ph.D.	Associate Professor, University of Ottawa 613-562-5800 x 1009
Dr. Laura Gaudet	Associate Scientist, Ottawa Hospital Research Institute 613-737-8899 x 76655
Martin Holcik, Ph.D.	CHEO Research Institute
David Grynspan, Ph.D.	CHEO Pathology
Shannon Bainbridge, Ph.D.	Ottawa Hospital Research Institute University of Ottawa
Jane Shearer, Ph.D.	University of Calgary
John T. Arnason, Ph.D.	University of Ottawa
Zach Ferraro, Ph.D.	University of Ottawa

Collaborators:

Dr. Natalie Gauthier	Hôpital Montfort
Jameason Cameron, Ph.D.	CHEO Research Institute
Dr. Liisa Honey	Queensway Carleton Hospital
Research Coordinator:	University of Ottawa 613-562-5800 x1012
Funding Agency:	Canadian Institute of Health Research (CIHR)

Participation in this study is voluntary. Please read this Participant **Informed** Consent Form carefully before you decide if you would like to participate. Please ask the principal investigator and the study team as many questions as you like. We encourage you to discuss your options with family, friends or your health care provider.

Why am I being given this form?

You are being asked to participate in this research study because you are pregnant and planning to deliver locally and have indicated that you are interested in learning more about our research study.

Why is this study being done?

The PLACENTA study is designed to look at how lifestyle behaviours during pregnancy can affect how nutrients move to the growing fetus. The placenta is an organ that forms during pregnancy to support the baby. The placenta controls the transfer of nutrients (sugar, protein and fat) and oxygen to the fetus, and removes waste. If the placenta is not working properly, the baby may receive too few or too many nutrients. It is not well known how health behaviours, like exercise or nutrition, affect the transfer of nutrients to the fetus.

The goal of this study is to see if there are differences in the placenta's ability to transfer nutrients in pregnant women who exercise regularly compared to women who do not exercise regularly. This study is an observational study, we do not want you to make changes to your lifestyle because you are part of this study. We are simply looking to observe the natural differences between people and the impact that those differences may have.

During pregnancy, the placenta plays an important role in the growth and/or overgrowth of the baby. Based on work done by our team and others we believe that healthy eating and physical activity will be linked to differences in:

A) The way that new blood vessels form from existing ones (in the way that your cells respond to oxygen)

B) In the way that nutrients and oxygen move across the placenta (both of which are key controllers of the baby's growth).

This study will compare samples of the placenta from women who were physically active throughout their pregnancy and those who were not. We will explore the impact of physical activity on the genes that control the transfer of nutrients across the placenta to the fetus. We will also analyze the nutritional, environmental, and genetic factors that may affect placenta function by studying the relationship between genes/DNA and natural processes that occur during pregnancy which determine how a baby grows while in the womb and after birth. Genes are the building blocks or instructions found inside cells, which contribute to the different features you have, such as the colour of your hair and eyes. We hope that the information we learn in this study will be helpful in designing preventive health strategies for pregnancy.

How is the study designed? What is expected of me?

If you consent to participate in this study, you will be asked to come to the University of Ottawa-Lees Campus to meet our research team once during each trimester at specific times and dates which will be arranged between you and the study's research coordinator. Our goal is to recruit a group of women in their first trimester of pregnancy and should you attend your first visit during your first trimester, you will attend three (3) visits in total. However, many women do not know that they are pregnant or see their doctor before their second trimester. If you are recruited in your second trimester, you will be asked to come for two (2) visits.

The first trimester visit will occur between weeks 12-16 of your pregnancy. The second trimester visit will occur between weeks 24-28 of your pregnancy. The third and final visit will occur between weeks 34-38 of your pregnancy. The estimated length of each visit is 1.5 hours. Visits will take place during the week or on the weekend at a time that is convenient for you.

Visit details: first, second and third trimester

These visits will take approximately 1.5 hours each.

1) A small fasting (no food for 8 hours before) blood sample (2 teaspoons or 10 ml) will be taken. It is best if we book your appointments for first thing in the morning, before you have eaten breakfast. This blood sample will be used to measure metabolic markers associated with nutrient transport, fetal growth, and weight gain.

2) After the blood sample, you be given a small snack, for example a granola bar and some juice (or you can bring your own snack).

3) You will be asked to complete a few questionnaires:
    a. Socio-demographic information (first visit only)
    b. General health behaviours
    c. Diet History Questionnaire (first visit only)
    d. Edinburgh Postnatal Depression Score

4) We will measure your height and weight.

5) We will then ask you to put on a heart rate monitor, and skin temperature sensor stickers and rest seated for 20 minutes in order to collect your resting energy requirements and heart rate. After the period of seated rest, we will ask you to walk on a treadmill at a comfortable pace (2 mph, 3.2 kph). The incline of the treadmill will increase every 3 minutes for approximately 20-25 minutes, but you can choose to stop at any point. At the end of each stage, we will ask you how hard you feel that you are working (Borg scale of perceived exertion), how hot you feel (thermal sensation scale), and we will measure your body temperature using an ear thermometer. We will measure your heart rate and stop the test before you reach 85% of their maximum estimated heart rate.

6) You will be asked to complete three 24-hour dietary recalls (food and drinks) in the week following each visit (2 week days, 1 weekend day), this will take about 20 minutes/day. You can do this online with information that we will give you, or on paper if you don't have access to the internet.

7) You will be given a small physical activity monitor to wear for 1-week after each visit. It is a 'smart' pedometer that works like the motion sensor (counting steps) but also provides

information on your speed and direction of movement. It is always on but it is activated only by movement. This will give us an idea of your typical physical activity habits. The monitor (1” square) is safe, relatively small, non-invasive and is worn on a soft belt around the waist either under or over clothing and will not impact day-to-day activities. While we hope that you treat your accelerometer responsibly, please note that in the case of loss or breakage of the physical activity monitor, you will not be responsible for costs of replacement.

8) In the week following the visit, you will be asked to collect a small stool sample using a collection kit that we will provide you. You will then mail the kit, the physical activity monitor, and the physical activity log sheet to our office in the pre-addressed, pre-stamped envelope that we will provide you.

Visit details: At birth and 24-48 hours post-birth:

This visit will take approximately 10 minutes.

1) When you arrive at the hospital/birthing unit in labour, please mention that you are part of our study. We will already have given the hospital/birthing unit a note in your file (and a door magnet) to indicate that you are participating in our study and to remind the hospital/birthing unit staff to call the research team for placenta sampling if you present at or greater than 37 weeks gestation. If you arrive in labour less than 37 weeks gestation, you will be excluded from the placenta sampling and infant measurements. The note will include your name, date of birth, the phone number to reach our research team, and brief sample processing directions for blood samples and placenta and will be kept in your paper file but not in your electronic online hospital file. We will not interact with you while you are in labour. The Labour and Delivery clerk or Midwife will call the research team to visit the hospital/birthing unit/home to pick up your placenta for sampling.

2) Once the placenta is no longer attached to you or your baby, the nursing staff or midwife will provide us with your placenta so that we can take a blood sample (5 –10mL or 1 - 2 teaspoons) from the umbilical cord, weigh the placenta and take tissue samples from it. This will not involve any pain and will not involve sticking your baby with a needle. These samples will be used to assess markers associated with nutrient transport, growth and development. Our sampling may prevent you from taking part in a private cord blood storage program. The blood sample that we store for research purposes will not be available to you for any other purposes.

3) We will return to the hospital 24 – 48 hours after you have your baby, to measure the infant's height, weight, and body composition (skin folds). If you have been released by the hospital by this time, we will visit your home for the very short assessment. We will confirm these details with you during your last visit at the Lees Campus.

4) Approximately one (1) week after you give birth, you will be asked to collect a small stool sample from yourself, as well as one from your baby, and place them into the special collection kits that we will have given to you. We will call you to remind you to send in

your samples. You will then mail the kit to our office in the pre-addressed, pre-stamped envelope that we will provide you.

5) Access to your medical charts from your delivery will be made through the service of clinical archives of the Montfort hospital or the Ottawa Hospital to obtain information on a variety of measures that are conducted and recorded as part of your standard care unrelated to the study. We will collect information such as your child's sex, date of birth, birth weight, crown-heel length, if your baby was born premature or at term, and APGAR scores. We will also retrieve information about you, including your age, height, weight and gestational age at the time of delivery, index of parity, the weight of your placenta, level of labour pain, method of delivery, recorded alcohol and drug consumption during

Table 1: Study Visits and Procedures

Boxes marked with an X show what will happen at each visit.

Visit	**1st trimester visit (weeks 12-16) Sub-sample early recruits only**	**2nd trimester visit (weeks 24-28) ALL participants**	**3rd trimester visit (weeks 34-38) ALL participants**	**Birth & Post Birth**
Length of time needed	1.5 hours	1.5 hours	1.5 hours	10 minutes with baby
Maternal height and weight	X	X	X	
Questionnaires	X	X	X	
Blood Sample	X	X	X	
Fitness Test	X	X	X	
Placenta processing				X (birth)
Infant length, weight and body composition				X (24 hrs post-birth)
Stool samples (Maternal all visits and post-birth) & Baby post-birth	X	X	X	X (1 week post-birth) X (baby)

If you are interested, you can choose to allow us to contact you for future research studies done by our study team related to health behaviours and pregnancy outcomes. This is not a mandatory part of your participation for this study. The signature page at the end of this document allows you to indicate your preference. Also, you will be asked to sign a separate consent form for any future research projects that you may optionally be contacted about and wish to participate in.

Will my samples be used in future research studies?

If you accept this optional component, any leftover blood/DNA and placenta tissue as well as leftover samples of your baby's blood/DNA will be stored for future research studies related to placenta function. The study of biology is rapidly evolving, as is our understanding of genetics and more notably something called 'epigenetics'. This is a relatively new area of research and simply put, epigenetics is the study of biological mechanisms that can switch genes on and off. For example, what you eat, where you live, who you interact with, when you sleep, how you exercise, and even aging can change the way our genes are turned on or off over time. Some of these changes can be inherited and the different combinations of genes that are turned on or off are what makes each one of us unique. We would like to have the opportunity to examine this further as it relates to behaviours in pregnancy. Research Ethics Board approval will be sought before any future research begins.

We will take the baby's sample from the umbilical cord once it is cut away from the baby after delivery and no longer attached to you or your baby. Similarly, the placenta tissue sample will be taken after it has been delivered and thus will not involve any pain whatsoever nor will these procedures involve sticking your baby with a needle.

All samples will be coded (they will not contain any of your personal identifying information) and will be kept in a locked –80°C freezer located Kristi Adamo's lab at the University of Ottawa-Lees Campus for an indeterminate period of time. All of your personal health information collected will be de-identified and associated with only a study ID number, however a password protected master list containing your name and study ID number will exist and be accessible only to the Clinical Research Coordinator conducting the study.

As recommended, all the samples will be owned and governed by the Principal Investigator, Kristi Adamo, Ph.D. In order to protect the biospecimen integrity, the samples will be kept in a locked –80°C freezer at the University of Ottawa, Lees Campus. Samples may be released to co-investigators to analyze with specialized equipment in their labs at CHEO, the University of Calgary, or other labs at the University of Ottawa. Further, samples may be released to external investigators conducting similar investigations as part of secondary analysis, under the guidance of Kristi Adamo, Ph.D. In the event of future research, samples will only be released following the approval of secondary analysis by the Research Ethics Board at the University of Ottawa. Kristi Adamo has been successfully funded for 8 years and will make every effort to ensure the long-term sustainability of the biobank. After having completed all of the analyses and stored for the appropriate duration, the University of Ottawa will take all unused blood samples and will destroy them according to their usual method.

How long will I be involved in the study?

Your participation in the study will last approximately 6 months or until delivery. Over this time, you will be required to visit the University of Ottawa-Lees campus, once per trimester of pregnancy, up to a total of 3 times.

What are the potential risks I may experience?

There is little risk to you or your baby by participating in this study.

Blood drawing causes some pain and may cause bruising, bleeding or infections at the site of the needle stick. A nurse or certified phlebotomist has been trained in safely drawing blood. Care will be taken to avoid theses complications.

The walking fitness test will occur in a safe environment and will incorporate the most recent evidence for exercise guidelines during pregnancy. CPR and first aid trained personnel, specially trained to perform exercise testing, will coordinate and monitor the testing. Heart rate will be continually monitored to ensure that you do not reach an unsafe heart rate. Research staff will make sure the treadmill is adjusted properly and will conduct a proper warm-up and cool-down to prevent injuries.

The risk of an adverse event is minimized through the supervision of testing by qualified personnel. In the unlikely event that you experience an injury, medical or psychological crisis (i.e. chest pains, heart attack, panic attack, etc.) during the fitness test, a safety protocol is in place and the university emergency response team will be contacted immediately.

The accelerometer has been approved by Health Canada as a medical device, however, it is small in size and as a result although unlikely, could pose a risk as a choking hazard to children under the age of 3 years old if it were to become detached from its accompanying belt. For this reason, the accelerometer should remain attached to the belt at all times and be worn only by the study participant.

Questionnaires:

You might not like all of the questions that you are asked. You do not have to answer any questions that make you uncomfortable.

If this study uncovers information that might be helpful to your current or future health, the Research Coordinator would offer to discuss these findings with you. The Research Coordinator would first advise you of any risks and benefits of sharing this information with you. If necessary, the investigator will recommend consultation with an appropriate medical professional (e.g. Clinical Psychologist).

Can I expect to benefit from participating in this research study?

The results of these tests may not be directly beneficial to you and your baby but the results will help define the potential role for physical activity in pregnancy, and the knowledge gained from this study may benefit other pregnant women in the future. The results from this study will be shared with health care professionals including general practitioners, obstetricians and gynecologists, exercise and nutrition professionals as well as policy makers and health care planners. At the end of the research study, you are provided the option to receive a summary of your results if you wish. The entire duration of the project is 5 years, therefore it could take over 5 years to receive your results.

Would you like to receive a summary of research results (please check the appropriate box)?

☐ Yes ☐ No

Do I have to participate? What alternatives do I have?

You can choose not to participate in this study. The alternative to this study is not to participate.

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later without affecting the medical care, education, or other services to which you are entitled or are presently receiving at this institution.

<u>If I agree now, can I change my mind and withdraw later?</u>

You may withdraw from the study at any time without any impact on your current or future care at the Ottawa Hospital, CHEO, Montfort Hospital, or Queensway Carleton Hospital.

- If you withdraw your consent, the study team will no longer collect your personal health information for research purposes and you will no longer be expected to attend the study visits.

Information and samples collected for the study before you cancel this consent may still be used unless you request for them to be destroyed. You have the right to request for them to be destroyed.

<u>What compensation will I receive if I am injured or become ill in this study?</u>

In the event of a study-related injury or illness, you will be provided with appropriate medical treatment and care. Financial compensation for lost wages, disability or discomfort due to an injury or illness is not available. You are not waiving any of your legal rights by agreeing to participate in this study. The Principal Investigator, the Ottawa Hospital, the Montfort Hospital, CHEO, the Queensway Carleton Hospital, the University of Ottawa and the University of Calgary still have their legal and professional responsibilities.

<u>Will I be paid for my participation or will there be any additional costs to me?</u>

You will not be paid to be a participant in the study; however, a parking voucher will be provided to you to cover bus or parking costs for all visits attended with the study team at the University of Ottawa-Lees Campus.

At the end of the study, you will be given the option to receive a general health fitness program developed by a certified exercise physiologist and supervised workout access at our private fitness facility at University of Ottawa – Lees Campus, Behavioural and Metabolic Research Unit. Access will be provided for 3 consecutive months post-partum, starting after you have recovered from the birthing process and within six months of the birth of your baby. Participation in this component is optional and only if you desire.

At the end of the study you will also be given a thank you card with a $50 gift certificate to either a grocery store, book store, or coffee shop (based on your preference) as a token of appreciation for your time to participate in the study visits.

How is my personal information being protected?

- All information and samples collected during your participation in this study will be identified with a unique study number, and will not contain information that identifies you, such as your name, address, etc.
- The link between your unique study number and your name and contact information will be stored securely, password protected and separate from your study records, at The University of Ottawa. The link will not leave the University of Ottawa.
- Any documents or samples leaving the University of Ottawa will contain only your unique study number. This includes publications or presentations resulting from this study.
- Your and/or your baby's medical record will be accessed. However, the information collected, as well as the placenta tissue and blood samples, which leave The Ottawa Hospital, CHEO, Montfort Hospital, or the Queensway Carleton Hospital, will only contain your unique study number.
- Information that identifies you will be released only if it is required by law.
- For audit purposes only, your and your baby's original medical records may be reviewed under the supervision of an investigator and/or their staff by representatives from:
    - the Ottawa Health Science Network Research Ethics Board (OHSN-REB)
    - the Ottawa Hospital Research Institute
    - CHEO Research Ethics Board
    - The Health Sciences and Science REB at the University of Ottawa
    - Montfort Research Ethics Board
    - University of Calgary Conjoint Health Research Ethics Board (CHREB)
    - The Queensway Carleton Hospital Research Ethics Board
- Research records will be kept for 10 years, as required by the OHSN-REB.
- At the end of the storage time, all paper records will be shredded and all electronic records will be securely deleted.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov. This website will not contain any information that identifies you. At most, the Web site will provide a summary of results. You can search this Web site at any time.

Do the investigators have any conflicts of interest?

The investigators have no conflicts of interest to declare related to this study.

What are my responsibilities as a study participant?

It is important to remember the following things during this study:

- Ask the research team if you have any questions or concerns.
- Tell the research team if anything about your health has changed.
- You should not eat or drink (except for water) for 8 hours before each visit so that we can obtain fasting blood samples. A snack will be provided immediately following the blood draw.

Who do I contact if I have any further questions?

If you have any questions about this study, please contact Kristi Adamo, Ph.D., at 613-562-5800 x 1009, Dr. Laura Gaudet at 613-737-8899 x 7665, or the study staff at 613-562-5800 x1012 or x7367.

The Ottawa Health Science Network Research Ethics Board (OHSN-REB), CHEO Research Ethics Board (CHEO REB), Hôpital Montfort Research Ethics Board, Queensway Carleton Hospital Research Ethics Board, University of Ottawa Research Ethics Board and the University of Calgary Research Ethics Board have reviewed this protocol. If you have any questions about your rights as a study participant, you may contact the Chairperson of the Ottawa Health Science Network Research Ethics Board at 613-798-5555, extension 16719, the Chairperson of the CHEO Research Ethics Board at 613-737-7600, extension 3272, the Hôpital Montfort Research Ethics Board Manager at 613-746-4621, extension 2221, the Queensway Carleton Hospital Research Ethics Board at (613) 721-2000 extension 1019, or the Office of Research Ethics and Integrity at the University of Ottawa at 613-562-5387.

PhysicaL ACtivity and diEtary implicatioNs Throughout pregnAncy (PLACENTA)

Consent to Participate in Research

- I understand that I am being asked to participate in a research study about physical activity and diet during pregnancy.
- This study was explained to me by ___________________________.
- I have read, or someone has read to me, each page of this Participant **Informed** Consent Form.
- All of my questions have been answered to my satisfaction.
- If I decide later that I would like to withdraw my participation and/or consent from the study, I can do so at any time.
- I voluntarily agree to participate in this study.
- I will be given a copy of this signed Participant **Informed** Consent Form.

Consent for the baby's participation

You accept that your newborn participates in this research conducted by Principal Investigator Kristi Adamo Ph.D.'s research team. I was explained all relevant aspects of the research and my questions were answered to my satisfaction. I was informed that my newborn's participation to this project is voluntary and can cease at any time without any form of penalty. I was given enough time to discuss with my family about the nature and involvement of my newborn in this project. I authorize the archives service to give to the research team only the information from my newborn's medical record mentioned above. I can withdraw my newborn from this project without having to provide a reason.

Please initial:

___ Yes	__ No	I realize that my participation is voluntary and I am free to withdraw from the study at any time.
___ Yes	__ No	Having my blood/DNA and placenta tissue samples stored and used for future ethics approved research on health behaviours (i.e. nutrition & physical activity), pregnancy outcomes and weight regulation.
___ Yes	__ No	Have my child's cord blood/DNA samples banked and used for future, ethics approved research on health behaviours (i.e. nutrition & physical activity), pregnancy outcomes and weight regulation.
___ Yes	__ No	To be contacted in the future for follow up studies

Contact Information:

Daytime telephone number(s): ______________________________

Evening telephone number(s): ______________________________

Email address: ______________________________

Alternate Email address: ______________________________

______________________ ______________________ ______________________

Name of Participant (Print) Signature of Participant Date

PhysicaL ACtivity and diEtary implicatioNs Throughout pregnAncy (PLACENTA)

<u>Assistance Declaration</u>

Was the participant assisted during the consent process? ❑ Yes ❑ No

❑ The consent form was read to the participant/substitute decision-maker, and the person signing below attests that the study was accurately explained to, and apparently understood by, and consent was freely given by the participant/substitute decision-maker.

❑ The person signing below acted as a translator for the participant/substitute decision-maker during the consent process. He/she attests that they have accurately translated the information for the participant/substitute decision-maker and believe that the participant/substitute decision-maker has understood the information translated.

______________________________ ______________________________ ______________________

Name of Person Assisting (Print) Signature Date

<u>Investigator or Delegate Statement</u>

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

______________________________ ______________________________ ____________________

Investigator/Delegate's Printed Name Investigator/Delegate's Signature Date

APPENDIX II: MODIFIED HALO SUBMAXIMAL EXERCISE TEST PROTOCOL

Date (dd/mm/yyyy) | ID number

		/			/	2	0			**HALO Submax Protocol**	P	L	A				T		

DOB (MMM-YY): **Age:**	**Height:** **Weight:** **Pre-instrumentation:** **Instrumented:**	**Predicted HRmax:** **85% HRmax:**
Room Temp: ______ ºC	**Relative Humidity: _________ %**	**Air Pressure: _______ pa**

Time (min)	**Test Time** (sec)	**Speed** (mph)	**Grade** %	**HR** (bpm)	**RPE**
Resting and seated					
0-1					
1-2					
2-3					
3-4					
4-5					
5-6					
6-7					
7-8					
8-9					
9-10					
10-11					
11-12					
12-13					
13-14					
14-15					
15-16					
16-17					
17-18					
18-19					
19-20					

Time (min)	Test Time (sec)	Speed (mph)	Grade %	HR (bpm)	RPE
0-4	**-4**	2	0		
4-7	**30 (0:30)**	2	2		
	60 (1:00)	2	2		
	90 (1:30)	2	2		
	120 (2:00)	2	2		
	150 (2:30)	2	2		
	180 (3:00)	2	2		
7-10	**30 (0:30)**	2	4		
	60 (1:00)	2	4		
	90 (1:30)	2	4		
	120 (2:00)	2	4		
	150 (2:30)	2	4		
	180 (3:00)	2	4		
10-13	**30 (0:30)**	2	6		
	60 (1:00)	2	6		
	90 (1:30)	2	6		
	120 (2:00)	2	6		
	150 (2:30)	2	6		
	180 (3:00)	2	6		
13-16	**30 (0:30)**	2	8		
	60 (1:00)	2	8		
	90 (1:30)	2	8		
	120 (2:00)	2	8		
	150 (2:30)	2	8		
	180 (3:00)	2	8		

Comments:

16-19	**30 (0:30)**	2	10				
	60 (1:00)	2	10				
	90 (1:30)	2	10				
	120 (2:00)	2	10				
	150 (2:30)	2	10				
	180 (3:00)	2	10				
19-22	**30 (0:30)**	2	12				
	60 (1:00)	2	12				
	90 (1:30)	2	12				
	120 (2:00)	2	12				
	150 (2:30)	2	12				
	180 (3:00)	2	12				
22-25	**30 (0:30)**	2	14				
	60 (1:00)	2	14				
	90 (1:30)	2	14				
	120 (2:00)	2	14				
	150 (2:30)	2	14				
	180 (3:00)	2	14				
Rec.	**0-1**	1	0				
Rec.	**1-2**	1	0				

Comments:

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Post- Trial Weight:

(Still instrumented)

__________ **Kg**

Description of Clothing:

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APPENDIX III: INDIRECT CALORIMETRY DATA COLLECTION PROTOCOL AND ANALYSIS

The rest and exercise portion of the experimental protocol take place in the metabolic chamber.

ExpeData Set-up:

Open ExpeData on the desktop, then follow the next steps:

- Select ‘Acquire’ and then ‘Setup Data Acquisition’
- Then click ‘Re-Scan Comm Ports’, then in the Universal Interface II (UI2) box, select ‘COM1’ in the drop-down menu. Click on ‘UI2’ and press ‘OK’.
- At the bottom left of the ‘Acquisition Parameter Box’ select ‘Channels’ in the top menu, and click ‘Set-up’, select the Protocol Folder and search file named Placenta_longertime.stp
- Check all the channels: O2: A=19, B=0.5; CO2: A=0, B=0.4; Flow: A=0, B=100; WV: A=0, B=1.
- Check the large green check mark.

Gas calibration:

- Set up pump drive to 5.5% (open loop) or ~250 mL/min (closed loop).
- Use the N2 and O2 (20.95%)/ CO2 (5.0%) mixed gas tanks secured against the wall.
- Turn on N2 gas – enough to feel the air gently on your lips. Then attach to the **RH-300** on the left sample flow line. Let the gas run until oxygen is stable for 10 mins.
- On the RH-300 adjust the WVP to zero manually (turn mode knob one click to the right to “Adjust Zero” then use the adjust knob to make small increments to “0”).
- Then on the Fox Box use the mode knob to “Zero CO2” (about 5 clicks to the right). Then click Enter (the red button next to the adjust knob). Once the CO2 value has stabilized (at least 1 min), turn “MODE” knob until “ADJUST CO2 SPAN”. Use the “ADJUST” knob to make the reading on the display match the CO2 value on the gas you are spanning (display should be 0.5000; get the gas to hover between 4.995 – 5.010). Press “ENTER” to confirm.
- Turn “MODE” knob until “FIXED OXYGEN SPAN 20.95%” appears. Press “ENTER” button to set the span oxygen span.
- Remove N2 gas and TURN OFF. Purge the line by close all three knobs all the way, starting with the big knob.

- Now attach the dry-rite to “Baseline". Water will “zero” then you will have a dry O2 sample. Write down the wet and dry O2% values, write the bp (kPa) value from the RH-300 (31 clicks to the right, bottom number, make sure to not click enter). Take the dry-rite off then using the mode knob on the Fox Box to “water span” (two clicks to the right) adjust the value according to the equation: bp*((O2dry-O2wet))/O2dry
- Turn on the gas mix (allow a light air flow). Then take the line from the gas tank and connect to the chamber port on the FoxBox.
- Ensure the switch between ‘Chamber’ and ‘Baseline’ is set to ‘Chamber’.
- On ExpeData select the Red Play button to begin gas measurement/calibration separately for N2 and O2/CO2 mixed gas. Ensure the gases measured reached stable values prior to adjusting and ending calibration.

Calibration complete:

- Turn off gas (make sure the large black knob is tightly closed, then wait to purge the line, then tightly close large/small blue knobs.
- On Expedata close the recording button (make sure to save the calibration in the calibration folder), then click ‘OK’ again to open a new recording.
- **Prior to data collection, ensure that the flow kits are set to the appropriate flow rate for your data collection (baseline/rest set at 100 L/min and exercise is set at 250 L/min).**

Data Collection:

- Run an ambient measure first of chamber air. Allow the ambient air to stabilize and run for approximately 15-20 minutes, then click ‘Pause’.
- When participant is connected to the mask and ready for resting/baseline measurement click ‘Play’. Record flow rate from the LifeWind.
- After the 20 minutes of rest/baseline, click ‘Pause’. While the participant prepares for exercise portion of experimental protocol, increase the flow kit to 250 L/min. Once participant is ready for exercise, click ‘Play’.
- As the exercise continues, ensure to place a ‘Marker’ for each increase in stage. After the recovery period and the participant has left the metabolic chamber, begin post-ambient measurement for the same approximate duration as the initial ambient measurement.
- Save the file as ‘PLA###T#_DD/MM/YYYY’.

Data Analysis:

- On Expedata click on ‘View’ – pick CO2 as the ‘Active Channel’. Then select a minimum of 200 samples in the ambient baseline. Then click on ‘Edit’ tab/Markers and insert markers with at least 200 samples between each marker, label with the letter ‘a’. For example, 215 a, 415 a, 615 a. Then click ‘On’ to see the markers.
- Then to ensure baseline CO2, FH2O and O2 all have the same time point. Click on ‘Transform’ – ‘Correction’ – ‘Lag Correction’. In the opened ‘Lag’ tab, first select ‘FH2O’ in the pacemaker channel. Then do the same steps but select ‘CO2’ and ‘O2’ active channels.
- After you have completed the lag correction for all channels (FH2O, CO2, O2), the next step is to run the set-up macros to correct for water vapour pressure (WVP) in MACRO 1, then run the following MACROS to calculate volume of oxygen/carbon dioxide (VO2/VCO2) and RER.
- To run the macros click ‘Tools’ – ‘Macro Utlility’- ‘Macro’ – Open macro collection labelled ‘Typical Analysis II’. Then click MACRO 1 and click green arrow.
- Then select a sample of the ambient baseline, then click on ‘Mean’-check ‘Start from K1’- then click ‘Execute’ and then ‘Exit’.
- Then select MACRO 2 and press the green arrow.
- At this point in the active channel you can display VO2, VCO2 and RER via the ‘View’ tab.
- Now you can extract the raw data in an excel file and calculate the means accordingly.

APPENDIX IV: CALIBRATION OF SYSTEMS

Propane Validation

To establish that the rate of VO2 and VCO2 values are accurate, we conducted a propane validation test. Propane was burned for 30-minutes and the mass was measured pre- and post- testing. Then the mass was used to calculate expected rates of VO2 and VCO2 based on their respective stoichiometry's which was then compared to values obtained during the combustion test. The differences between expected values measured for the rates of VO2, VCO2 and the RER were less than 10%.

Treadmill Calibration

The treadmill speed and incline were calibrated to ensure appropriate measurements of metabolic heat production were completed.

Speed Calibration:

- Length of the belt was measured by marking each consecutive metre with tape until the starting point. Then count the number of revolutions completed over 60-seconds while the treadmill was running at a speed of 3.2 km/h.
- The total horizontal distance travelled was calculated by multiplying measured belt length by the revolutions per minute. Where, distance (metres) = speed (metres per second) x time (seconds).

Incline of the Treadmill:

- Height of the treadmill was measured from the initial 0% grade position, then at every 2% incline up to 14%.
- Then to get the change in height, the difference final and initial height was calculated.
- Then the tangent of that height was calculated to get the accurate % incline.