A single bout of discontinuous exercise as a pragmatic approach to augment glycaemic control in pregnancy: a pilot study

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*University of Wollongong*

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A SINGLE BOUT OF DISCONTINUOUS EXERCISE AS A PRAGMATIC APPROACH TO AUGMENT GLYCAEMIC CONTROL IN PREGNANCY: A PILOT STUDY

A thesis submitted in partial fulfilment of the requirements for the award of the degree

Master of Science

from the

UNIVERSITY OF WOLLONGONG

by

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Bachelor of Exercise Science and Rehabilitation (Hon)

Centre of Human and Applied Physiology
School of Medicine

Supervisors: Dr. Herbert Groeller and Dr. Theresa Larkin

2017
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>BGL</td>
<td>Blood glucose level</td>
</tr>
<tr>
<td>BGM</td>
<td>Blood glucose monitor</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CGM</td>
<td>Continuous glucose monitoring</td>
</tr>
<tr>
<td>CV (%)</td>
<td>Coefficient of variation (percentage)</td>
</tr>
<tr>
<td>EPOC</td>
<td>Excess post-exercise oxygen consumption</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational diabetes mellitus</td>
</tr>
<tr>
<td>HF</td>
<td>High frequency spectral power</td>
</tr>
<tr>
<td>HR</td>
<td>Heart rate</td>
</tr>
<tr>
<td>HRR</td>
<td>Heart rate reserve</td>
</tr>
<tr>
<td>HRmax</td>
<td>Maximum heart rate</td>
</tr>
<tr>
<td>HRV</td>
<td>Heart rate variability</td>
</tr>
<tr>
<td>IPAQ</td>
<td>International Physical Activity Questionnaire</td>
</tr>
<tr>
<td>L.min⁻¹</td>
<td>Litres per minute</td>
</tr>
<tr>
<td>LF</td>
<td>Low frequency spectral power</td>
</tr>
<tr>
<td>LF/HF</td>
<td>Ratio of low frequency to high frequency power</td>
</tr>
<tr>
<td>mmol.L⁻¹</td>
<td>Millimoles per litre</td>
</tr>
<tr>
<td>ms</td>
<td>Millisecond</td>
</tr>
<tr>
<td>n.u.</td>
<td>Normalised units</td>
</tr>
<tr>
<td>N/A</td>
<td>Not applicable</td>
</tr>
<tr>
<td>pNN50</td>
<td>Percentage of successive RR intervals that differ by &gt;50ms</td>
</tr>
<tr>
<td>RER</td>
<td>Respiratory exchange ratio</td>
</tr>
<tr>
<td>RMSSD</td>
<td>Root mean square of successive difference between RR intervals</td>
</tr>
<tr>
<td>RPE</td>
<td>Rating of perceived exertion</td>
</tr>
<tr>
<td>RPM</td>
<td>Revolutions per minute</td>
</tr>
<tr>
<td>R-R</td>
<td>Interval between successive QRS complexes</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SDNN</td>
<td>Standard deviation of all RR intervals</td>
</tr>
<tr>
<td>$\dot{V}_E$</td>
<td>Minute ventilation</td>
</tr>
<tr>
<td>VLF</td>
<td>Very low frequency spectral power</td>
</tr>
<tr>
<td>$\dot{V}O_2$</td>
<td>Oxygen consumption</td>
</tr>
<tr>
<td>$\dot{V}O_{2\text{max}}$</td>
<td>Maximum oxygen consumption</td>
</tr>
<tr>
<td>$\dot{V}O_{2\text{peak}}$</td>
<td>Peak oxygen consumption</td>
</tr>
</tbody>
</table>
ABSTRACT

Introduction: Pregnancy is a state of naturally occurring insulin resistance; with hyperglycaemia being associated with maternal and foetal risk for adverse outcomes. For women with a healthy pregnancy, Australian guidelines recommend regular moderate intensity exercise. However, many pregnant women report significant barriers for regular exercise participation, including misconceptions with respect to the safety of engaging in moderate and higher intensities of exercise. Interval exercise at high intensity is efficacious for glycaemic control in people with metabolic conditions such as type 2 diabetes. Yet in pregnancy, the effectiveness of a bout of interval (discontinuous) exercise on enhancing daily glycaemic control has not yet been investigated. Aim: This study investigated the effects of two different structured bouts of acute cycling (discontinuous with intermittent rest period vs. continuous) on acute cardiometabolic responses and 24-hour glycaemic responses in pregnant and non-pregnant women. Methods: Fourteen pregnant and non-pregnant women completed two exercise trials completed in a non-randomised format over consecutive weeks, with either a 30-minute bout of continuous or discontinuous exercise, matched for total external work. Acute cardiometabolic responses to exercise were measured immediately prior to, during and immediately after exercise, including blood glucose (BGL), expired gas exchange (oxygen consumption, respiratory exchange ratio and minute ventilation), and heart rate variability. Daily glycaemic responses were measured by continuous glucose monitor over 48-hours (24 hours either side of the exercise bout). Dietary and physical activity patterns were standardised between each 48-hour collection period. Results: Baseline BGL did not differ between pregnant and non-pregnant women and were within the clinically normal range. A significant interaction between exercise type and acute BGL changes immediately post-exercise was observed in pregnant and non-pregnant participants. In pregnant women, discontinuous exercise acutely lowered BGL by 4.8%, from 5.67mmol.L-1 (with 95% CI 5.24,6.10) to 5.40mmol.L-1 (4.82,5.97) (p= 0.008); while continuous exercise lowered BGL by 4.9%, from 5.24mmol.L-1 (4.85,5.63) to 4.98mmol.L-1 (4.59,5.38) (p= 0.020). In non-
pregnant women, acute BGL lowered by 8.2% after continuous exercise (5.58mmol.L-1 [4.62,6.55] to 5.16mmol.L-1 [4.39,5.81]) \( (p = 0.012) \); but only 1.8% after discontinuous exercise, which did not reach significance (5.60mmol.L-1 [5.05,6.15] to 5.50mmol.L-1 [5.01,5.99]) \( (p=0.175) \). Neither discontinuous \( (p=0.81) \) or continuous \( (p=0.21) \) exercise resulted in a significant interaction between 24h glycaemic responses and pregnancy condition. Similarly, there were no interactions observed for other cardiometabolic measures obtained during exercise, being heart rate variability differences that could reflect sympathetic and parasympathetic modulation, or metabolic measures that could reflect substrate utilisation during exercise. **Conclusion:** A bout of discontinuous, moderate intensity exercise totaling 15 min was equivalent to exercising for 30 minutes continuously at low intensity exercise for effects observed on acute post-exercise BGL response in pregnant participants. However, neither bout resulted in changes to measures of daily blood glucose control; nor differences in other cardiometabolic measures that could reflect differences of interval-structured exercise effect in pregnant participants. Further research is needed to identify a discontinuous exercise dose that augments daily glycaemic control in pregnancy and is well tolerated by pregnant women for regular participation in line with pregnancy recommendations.
ACKNOWLEDGEMENT

To my wonderful supervisors Herb Groeller and Theresa Larkin, a simple ‘thank you’ just doesn’t seem sufficient for how grateful I am for all that you have taught me and supported me through, the laughs shared and the positivity shown at times when they were most needed (and also for staying up late on my behalf on a school night). Thank you for letting me go and reigning me in at the same time – you found the perfect balance.

To the women who volunteered their precious time and energy to pedal their way through my study, I sincerely thank you for sharing your experiences with me and giving your time to allow me to do this work. Chatting with you added another dimension of learning to this degree and gave me much food-for-thought for my future endeavours.

Thanks to my friends and colleagues Marc Brown and Deirdre McGhee for propping me up with laughs, coffee and tea (and of course, biscuits), but most of all for giving me the space to finish this off. And to my fellow students in the Centre of Human and Applied Physiology, thanks for your shared wisdom and help in the lab.

Finally, to my wife Kate and my amazing friends and family – thanks for the endless love, support, practical advice, humour and cooking throughout this adventure. A special thanks to Anto for the countless times you let me ruin a perfectly good sunrise walk while talking things through about my study and my thesis, and for Bec, for your endless enthusiasm and support for my study and my ideas.

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PUBLICATIONS


CHAPTER ONE:
INTRODUCTION

THE ROLE OF ACUTE EXERCISE IN ENHANCING
GLYCAEMIC CONTROL IN PREGNANCY
1. THE ROLE OF ACUTE EXERCISE IN ENHANCING GLYCAEMIC CONTROL IN PREGNANCY

Regular exercise is strongly recommended during pregnancy for gestational health, including the management of glycaemic control and metabolic health (Artal 2015, Harrison, Shields et al. 2016, Hayman, Brown et al. 2016). Recently updated Australian recommendations advocate for regular moderate intensity exercise as the minimum level for women with a healthy, uncomplicated pregnancy (Hayman, Brown et al. 2016). Yet pregnant women face barriers for regular exercise participation, including adverse pregnancy symptoms (fatigue, nausea, mobility, comfort), a lack of confidence to commence or continue exercise safely during pregnancy, and uncertainty of benefit of doing exercise and moderate (or higher) intensities. These barriers, in part, contribute to 60-70% women being insufficiently active for health benefits. (Evenson and Bradley 2010, Cioffi, Schmied et al. 2010, Gjestland, Bø et al. 2013, Sui, Turnbull et al. 2013, Coll, Domingues et al. 2017). Recent reviews identified that women’s regular exercise participation reduces in pregnancy compared to pre-pregnancy, and further reduces with advancing gestation (Poudevigne and O’Connor 2006, Gaston and Cramp 2011). Furthermore, the intensity, frequency and duration of women’s exercise during pregnancy commonly decrease compared with pre-pregnancy (Poudevigne and O’Connor 2006, Gaston and Cramp 2011). This relative reduction in exercise associated with pregnancy and advancing gestation is counterproductive to the management of metabolic health, as it is in opposition to the progressive increase in maternal insulin resistance. Given this mismatch between recommended exercise for pregnancy health, including the management of hyperglycaemia, and exercise behaviours and beliefs during pregnancy, there is still a clear need for finding practical and effective exercise strategies to support glycaemic control that are also acceptable and non-threatening to women during pregnancy.

In non-pregnant persons at-risk of or diagnosed with metabolic dysfunction, exercise performed as an acute bout or as a chronic training regimen is well established as an effective treatment to reduce acute hyperglycaemia and improve long term glycaemic control (Boulé, Weisnagel et al. 2005, Praet, Manders et al. 2006, van Dijk, Tummers et al. 2012, Ruchat and Mottola 2013, Harrison, Shields et al. 2016, Colberg 2017). As an acute stimulus, exercise
promotes the uptake of glucose at skeletal muscle through both insulin-mediated and contractile-mediated (insulin-independent) mechanisms (Burstein, Epstein et al. 1990, Wright, Hucker et al. 2004, Hawley and Lessard 2008). In type 2 diabetes, skeletal muscle is a key regulatory tissue affected by peripheral insulin resistance and the adaptive response of skeletal muscle to acute exercise in type 2 diabetes participants enhances glucose uptake and insulin sensitivity (Devlin and Horton 1985, Goodyear and Kahn 1998). Beyond immediate acute effects following exercise, a single bout of moderate-intensity exercise has also been shown to significantly improve glycaemic control over a 24-hour period in obese and type 2 diabetic participants (Larsen, Dela et al. 1997, Praet, Manders et al. 2006, Bacchi, Negri et al. 2012, MacLeod, Terada et al. 2013, Van Dijk, Manders et al. 2013, Oberlin, Mikus et al. 2014). For pregnancy, a naturally occurring diabetogenic state, skeletal muscle has also been identified as the primary site for peripheral insulin resistance (Leturque, Burnol et al. 1984, Kuhl 1991, Sorenson and Brelje 1997, Barbour, McCurdy et al. 2007). Therefore, it is important to identify if an acute bout of exercise in pregnancy will have similar effects on acute glucose uptake and glycaemic control, that has been established in the type 2 diabetes literature. Early pregnancy studies have demonstrated exercise-related reductions in blood glucose in the acute post-exercise period (Bonen, Campagna et al. 1992, Lotgering, Spinnewijn et al. 1998, Bessinger, McMurray et al. 2002). Surprisingly, there have been no recent investigations evaluating the effectiveness of any type of acute exercise on blood glucose responses over a 24-hour period; despite the increasing prevalence of gestational diabetes (GDM), and recognised health risks associated with mild hyperglycaemia levels below GDM diagnostic thresholds (Waters, Dyer et al. 2016).

In terms of key exercise variables that are important for eliciting positive changes in glycaemic responses, both exercise intensity and total energy expenditure have been highlighted within the type 2 diabetes literature (Larsen, Dela et al. 1999, Praet and van Loon 2007, Grace, Chan et al. 2017). The use of discontinuous exercise structure, commonly referred to as interval exercise, is a physical loading strategy that allows for intermittent exposure to higher exercise intensities for a relatively short period of time, followed immediately by a period of rest or relative rest (light intensity work). The overall benefits of interval exercise, whether acute bout
or training, have often centred upon demonstrating comparable or advantageous physiological adaptations to more traditional continuous exercise, but with a reduced total exercise volume and/or duration needed to achieve the adaptation (Burgomaster, Howarth et al. 2008, Bartlett, Hwa Joo et al. 2012, Foster, Farland et al. 2015). To apply the interval exercise concept pregnant women, particularly those who are at higher risk for metabolic dysfunction such as hyperglycaemia or GDM, there needs to be practical consideration for the reported barriers to exercise that women experience, such as fatigue, physical discomfort, uncertainty around commencing exercise during pregnancy for previously inactive women, or uncertainty around safety of different intensities of exercise during pregnancy. Studies on the effects of interval exercise in obese or type 2 diabetes participants predominantly use intervals of high or supra-maximal intensity, commonly termed High Intensity Interval Training/Exercise (HIIT). There have been no studies at this stage evaluating HIIT in pregnant women for glycaemic control. Of important consideration is that the safety and acceptability of HIIT for women not active prior to pregnancy, or who have received a diagnosis of GDM or mild hyperglycaemia dysfunction, is unknown. Therefore, a discontinuous exercise protocol performed at moderate intensity would to be an appropriate and practical initial design to investigate efficacy on glycaemic responses in pregnant women. For the purpose of this thesis, the term ‘Discontinuous’ will be used when referring to interval exercise that is performed at moderate intensity, rather than the traditional high intensity design.

Whilst there are clear and beneficial findings when using the highest intensities of exercise in people who are healthy, or who experience obesity, type 2 diabetes, or metabolic syndrome (Gibala, Little et al. 2006, Burgomaster, Howarth et al. 2008, Tjonna, Lee et al. 2008, Hood, Little et al. 2011, Little, Gillen et al. 2011, Bartlett, Hwa Joo et al. 2012, Karstoft, Winding et al. 2014, Little, Jung et al. 2014), there has been little investigation of discontinuous exercise performed at a lower relative intensity for effects on glycaemic measures, compared to a continuous exercise protocol. To date, there has also been no studies evaluating the effects of an acute bout of discontinuous exercise of any intensity on any cardiometabolic measures in pregnant women. Therefore, this study aims to compare the effects of a discontinuous bout of exercise on glycaemic and cardiometabolic responses in pregnant women, compared to a
continuous bout of exercise, matched for total work performed. This will also be compared against a control group of pregnant women, to identify any possible pregnancy-specific responses that may inform further investigations and future studies. For this study, cycling was utilised as the mode of exercise primarily as it can be well-controlled for total work, which facilitates more specific comparison of the effects of continuous versus discontinuous exercise, and associated intensities, and not the overall energy expenditure of the exercise. Cycling also removes the influence of bodyweight on metabolic demands of the exercise and reduces potential issues of mobility and discomfort barriers which are important factors when investigating pregnant women at different stages of gestation, and different baseline bodyweights prior to pregnancy.

1.1 Aims and hypotheses:

This study aimed to investigate the effects of a single bout of discontinuous exercise on acute blood glucose and cardiometabolic exercise responses, and on daily glycaemic control in pregnant women. This was compared with responses to a bout of continuous exercise, matched for total work; and both protocols were also conducted in a control group of healthy, non-pregnant women. It was hypothesised that:

1. A bout of discontinuous, moderate intensity cycling will elicit comparable acute glycaemic effects to a bout of continuous, low intensity cycling of matched total work in pregnant women; with similar responses observed in the non-pregnant control group.

2. A bout of discontinuous, moderate intensity cycling will elicit different cardiometabolic responses during exercise and in the immediate post-exercise recovery period in pregnant women, compared with continuous, low intensity exercise.

3. In pregnant women, a bout of discontinuous, moderate intensity cycling will reduce 24-hour blood glucose levels and variability after exercise compared with 24-hours preceding exercise. Comparatively, there will be no effect observed in pregnant women following a bout of continuous, low intensity exercise; or in non-pregnant controls following either discontinuous or continuous protocols.
A fourth hypothesis (below) was added following data collection and review of the raw 24-hour blood glucose data. Both the pregnant and non-pregnant groups were found to be within normal clinical levels for all measured glycaemic responses, despite the pregnant group containing four women with diagnosed GDM, and the three non-GDM pregnant women having characteristics that would increase the likelihood of early peripheral insulin resistance and maternal hyperglycaemic, being high BMI and inactive prior to and during pregnancy. Based on there being no difference in baseline blood glucose levels across the participants, an analysis of pooled data was done to compare the effects of the two exercises, independent of pregnancy status. This is not the primary focus of the thesis but does allow for further evaluation of a discontinuous exercise bout done at moderate intensity compared with continuous, low-intensity exercise.

4. In participants with normal daily glycaemic levels, a bout of discontinuous moderate intensity cycling will elicit comparable acute and 24-hour blood glucose responses, compared to a bout of continuous, low intensity exercise of equal total work, but double the volume of exercise.
CHAPTER TWO:

REVIEW OF THE RELATED LITERATURE
2. REVIEW OF RELATED LITERATURE

This literature review will address several key areas of pregnancy and metabolic physiology that have been considered when identifying and defining the need and design of this study. Specific to pregnancy, this includes review of normal and abnormal metabolic changes in pregnancy; the adverse effects of poor maternal glycaemic control on cardiometabolic responses in both mother and offspring; the current challenges that beliefs and behaviours of pregnant women provide in utilising exercise as a strategy for improving glycaemic control; and the role exercise could play in improving maternal metabolic function. This review also explores some of the historical and current evidence that has established exercise as an effective treatment for glycaemic management in other metabolic populations; the dose and key variables that have been shown to drive glucose uptake and glycaemic regulation; and lastly to explore the role of interval (versus continuous) exercise, the physiological and practical benefits reported in the HIIT and SIT literature, and how these concepts may be an effective strategy for designing exercise to improve glycaemic control in pregnancy.

2.1 Metabolic changes in human pregnancy

During pregnancy, there are significant changes in maternal endocrine, cardiovascular, respiratory and metabolic functions as a natural adaptation of the gestational process to support the developing foetus (Lotgering, Gilbert et al. 1985, Clapp, Seaward et al. 1988, Barbour, McCurdy et al. 2007). The autonomic nervous system is directly implicated in these functions. During pregnancy, resting sympathetic drive is increased which results in relatively greater sympathetic modulation and lower parasympathetic control (Ekholm, Hartiala et al. 1997, Lucini, Strappazzon et al. 1999, Avery, Wolfe et al. 2001, Maser, Lenhard et al. 2014). At rest, maternal energy expenditure (oxygen consumption), respiratory demand (minute ventilation), and cardiac output (as a product of increased heart rate and stroke volume) are all elevated and continue to increase with advancing gestation (Lotgering, Gilbert et al. 1985, Artal, Wiswell et al. 1986). Therefore, overall cardiometabolic demands are increased as a function of normal healthy pregnancy.
The changes associated with higher metabolic demand and progressive insulin resistance in pregnancy are complex. Skeletal muscle has been identified as the primary site for maternal peripheral insulin resistance (Leturque, Burnol et al. 1984, Kuhl 1991). During pregnancy, resting glucose uptake in skeletal muscle is reduced as a method of conserving circulating maternal glucose to ensure foetal supply and growth demands are always met (Buchanan, Metzger et al. 1991, Catalano, Tyzbir et al. 1993, McMurray, Mottola et al. 1993, Catalano, Huston et al. 1999, Handwerger and Freemark 2000, Bessinger, McMurray et al. 2002, Barbour, McCurdy et al. 2007). Further, the synchronisation of the sympathetic nervous system and endocrine systems has significant influence on the maintenance of normal blood glucose at rest and during exercise (Suh, Paik et al. 2007). Therefore, there is also complex interplay between sympathetic and endocrine functions during pregnancy in terms of insulin resistance and glycaemic control.

2.1.1 Importance of glycaemic control
Progressive peripheral insulin resistance over the course of the gestational period is caused by the normal metabolic effects of circulating pregnancy hormones (Buchanan 1994, Sorenson and Brelje 1997). When the metabolic challenges of pregnancy trigger declining glycaemic control and cause maternal hyperglycaemia above the clinical target thresholds for optimal pregnancy glycaemic control (Nankervis, McIntyre et al. 2013, Waters, Dyer et al. 2016), this is termed gestational diabetes mellitus (GDM). Gestational diabetes is associated with a number of obstetric risks, including pre eclampsia, infection, caesarean delivery, and post-partum haemorrhage (Jovanovic and Pettitt 2001, Al-Qahtani, Heath et al. 2012, Lassi and Bhutta 2013). Furthermore, GDM is strongly associated with post-partum metabolic changes that can advance to chronic metabolic dysfunction in both mother and offspring. There is significantly elevated maternal risk for progression to type 2 diabetes mellitus and recurrence of GDM in subsequent pregnancies; and increased risk in offspring for obesity, type 2 diabetes, and GDM in females in later life (Moses 1996, Kim, Newton et al. 2002, Simeoni and Barker 2009, Mitanchez, Zydorczyk et al. 2015). This intergenerational effect of GDM has been identified as a critical contributor to progressive increases in the prevalence of both obesity and diabetes (Wild, Roglic et al. 2004, Moore 2010, Artal 2015).
Importantly, even mild levels of hyperglycaemia in pregnancy without a diagnosis of diabetes are still correlated with higher risks for adverse maternal and foetal outcomes (Metzger, Lowe et al. 2008, Moses, Morris et al. 2011, Waters, Dyer et al. 2016). Maternal hyperglycaemia increases the availability of circulating glucose to the foetus, via facilitated glucose diffusion across the placenta. Maternal insulin does not cross the placenta, and foetal insulin production does not occur until the later stages of development, thus maternal hyperglycaemia leads to a parallel hyperglycaemic state in the foetus, and at later stages, foetal hyperinsulinemia. In-utero, insulin has an important role as a growth hormone; therefore foetal hyperinsulinemia can potentially contribute to adverse birth outcomes, such as macrosomia, and neonatal hypoglycaemia (Aerts and Van Assche 2006, Hawdon 2008).

2.2. Exercise recommendations, beliefs and barriers in pregnancy

Regular exercise is strongly recommended for maternal health, including the prevention and management of gestational diabetes (Artal 2015, Harrison, Shields et al. 2016, Hayman, Brown et al. 2016). Recently revised Australian guidelines state that regular exercise performed at least at moderate intensity is the minimum level recommended for all women with a healthy pregnancy (Hayman, Brown et al. 2016). For inactive pregnant women, including those who were inactive prior to pregnancy, the guidelines also support the recommendations to commence with lower intensity activities, and potentially for short duration (15 minutes), with progression towards regular exercise of moderate intensity (Zavorsky and Longo 2011, Artal 2016, Hayman, Brown et al. 2016).

Many pregnant women face a number of barriers for regular exercise participation, including symptoms, mobility, and misconceptions around benefits of exercise at moderate or high intensity and exercise safety for commencing or continuing exercise during pregnancy (Evenson and Bradley 2010, Cioffi, Schmied et al. 2010, Coll, Domingues et al. 2017). Consequently, many pregnant women do not meet the minimum exercise recommendations (Gjestland, Bø et al. 2013, Sui, Turnbull et al. 2013). Recent reviews on beliefs and behaviours with respect to exercise during pregnancy have identified that regular exercise participation
is reduced at the onset of pregnancy, and continues to decline as gestation progresses (Poudevigne and O'Connor 2006, Evenson and Bradley 2010, Gaston and Cramp 2011). Furthermore, the intensity, frequency and duration of any exercise undertaken have all been found to decrease during pregnancy, compared to pre-pregnancy exercise behaviours, and further reduce within the third trimester compared with the first trimester (Poudevigne and O'Connor 2006, Gaston and Cramp 2011). Given the mismatch between the exercise that is needed for pregnancy health, including for management of glycaemic control and cardiometabolic changes, and the exercise behaviours and beliefs still held by many women during pregnancy, there remains a clear need to identify practical exercise strategies that are acceptable and non-threatening to pregnant women, and clinically effective in managing pregnancy-related health changes, and of particular interest to the primary aim of this study, glycaemic control.

### 2.2.1 Role of exercise in addressing maternal metabolic dysfunction

Exercise is one of the established essential therapies for the prevention and management of type 2 diabetes (Boule, Haddad et al. 2001, Colberg 2017). Yet the utilisation of exercise as a primary therapy for glycaemic control in pregnancy, including in GDM, remains limited. This is largely due to a lack of conclusive evidence from studies done so far, where the varying methods and different measures of glycaemic control used makes comparisons across the literature challenging, and the effects of exercise training on glycaemic measures reported are inconsistent and not strong enough to determine exercise dose needed for glycaemic improvement in pregnant women who are at-risk or diagnosed with GDM (Boule, Haddad et al. 2001, Metzger, Buchanan et al. 2007, Ruchat and Mottola 2013, Colberg 2017). The outcomes from prevention-focused studies indicate that higher levels of physical activity during the pre-pregnancy period or within the first 20 weeks of pregnancy are more likely to reduce GDM risk. Whereas, targeted exercise intervention studies aiming to improve the prevention of gestational diabetes have not been conclusive (Dye, Knox et al. 1997, Dempsey, Butler et al. 2004, Zhang, Solomon et al. 2006, Tobias, Zhang et al. 2011, Oostdam, Van Poppel et al. 2012, Barakat, Pelaez et al. 2013, Yin, Li et al. 2014). Looking at the evidence for exercise in managing GDM once women are diagnosed, there are a larger number of reviews on the
role of exercise in GDM than the number of actual studies conducted to measure the effects of exercise (acute bout or chronic training). Overall, chronic exercise interventions have had positive outcomes in GDM women, but with mixed and inconsistent results that relate to differing measures of glycaemic control (Jovanovic-Peterson, Durak et al. 1989, Avery, Leon et al. 1997, Brankston, Mitchell et al. 2003, Davenport, Mottola et al. 2008, de Barros, Lopes et al. 2010). A recent systematic literature review of GDM exercise intervention studies concluded that regular moderate intensity exercise (aerobic or resistance-based), performed at least three times per week, is both safe and effective for enhancing glycaemic control in women with diagnosed gestational diabetes (Harrison, Shields et al. 2016).

Due to the limited studies currently available, there remains a large gap in understanding the specific mechanisms of how exercise acutely affects glucose uptake and daily glycaemic control in both normal pregnancy and those with GDM. To date, there has been considerable reliance on the exercise effects that have been established in type 2 diabetes to inform exercise approaches for management of metabolic dysfunction and diagnosed GDM. The underlying physiology of peripheral insulin resistance is similar across pregnancy, GDM and type 2 diabetes; however, the insulin resistance in pregnancy is a normal and necessary physiological process, as opposed to the abnormal pathophysiology seen in type 2 diabetes. Further, the causes of beta-cell dysfunction in GDM are not yet well defined or understood (Bung and Artal 1996, Buchanan and Xiang 2005, Demirci, Ernst et al. 2012). Therefore, the role and effect of exercise in pregnancy, and in GDM, on peripheral insulin resistance and glycaemic responses may not be the same as established in type 2 diabetes. On the other hand, skeletal muscle is the primary site for the peripheral insulin resistance that occurs in pregnancy and in type 2 diabetes (Leturque, Burnol et al. 1984, Barbour, McCurdy et al. 2007). This is significant because of the two primary treatments currently utilised in pregnancy to manage glycaemic control, being specialised dietary intervention and insulin therapy, neither act directly on the skeletal muscle site. Physiologically, the use of exercise as a stimulus acting on skeletal muscle to augment glucose uptake should be an effective component for glycaemic control in pregnancy. Currently, the required dose and key variables to optimise exercise effect in pregnancy glycaemic control are not known.
Early studies reporting on the acute effects of a single bout of exercise in pregnant women were all performed using a continuous structure, with most using a cycle ergometer as the mode (Guzman and Caplan 1970, Sady, Carpenter et al. 1989, Artal, Masaki et al. 1990, Bonen, Campagna et al. 1992, Jaque-Fortunato, Wiswell et al. 1996, Lesser, Gruppuso et al. 1996, Avery and Walker 2001). A number of these studies reported on cardiovascular and metabolic gas exchange responses during and post-exercise, in addition to acute glycaemic changes; with a few also measuring sympathetic control and substrate utilisation. These are physiological factors that can have secondary effects on glycaemic levels and are known to be different at rest between pregnant and non-pregnant women. Therefore, the present study included measures of heart rate variability and metabolic gas exchange, in addition to glycaemic responses, to be able to provide a more comprehensive picture of the effects of discontinuous exercise compared to continuous exercise in pregnant women. The exercise mode of cycling was chosen, as it allowed for more appropriate comparison to the early pregnancy literature and provided an accurate method for controlling the total work (representative of metabolic cost, and energy expenditure) performed in each protocol such that it could be equally matched.

2.3 **Exercise - a potent stimulus for glycaemic control**

In non-pregnant study populations, exercise is a well-established treatment for reducing hyperglycaemic blood levels and improving daily glycaemic control in persons at-risk of or diagnosed with metabolic dysfunction (Boulé, Weisnagel et al. 2005, Praet, Manders et al. 2006, Praet and van Loon 2007, Colberg, Sigal et al. 2010, van Dijk, Tummers et al. 2012, MacLeod, Terada et al. 2013, Ruchat and Mottola 2013, Qiu, Cai et al. 2014). Previous investigations have demonstrated that the glucose regulatory effects of exercise take place at the skeletal muscle, the primary tissue affected by chronic peripheral insulin resistance (Devlin and Horton 1985, Goodyear and Kahn 1998). As an acute stimulus, exercise facilitates enhanced glucose uptake at skeletal muscle by mechanisms that are both insulin-mediated and independent of insulin via muscle contraction (Burstein, Epstein et al. 1990, Wright, Hucker et al. 2004, Hawley and Lessard 2008). Specifically, a single bout of exercise augments glycaemic control through several mechanisms, including: enhanced glucose uptake in
skeletal muscle via increased GLUT4 translocation and GLUT4 mRNA expression; increase activity of skeletal muscle AMP-activated protein kinase (AMPK); regulation of other proteins involved in insulin signalling pathways; increasing the oxidative capacity of skeletal muscle; and acute muscle glycogen depletion (Houmard, Hickey et al. 1995, Kennedy, Hirshman et al. 1999, Kuo, Browning et al. 1999, Chen, Stephens et al. 2003, Kranio, Cameron-Smith et al. 2006, Sriwijitkamol, Coletta et al. 2007, O’Neill 2013). In pregnancy, however, the peripheral insulin resistance is not a pathophysiological process of metabolic dysfunction, but rather a naturally occurring biological mechanism that ensures adequate blood glucose supply is available to the developing foetus (Buchanan 1994, Sorenson and Brelje 1997). Therefore, it is not yet known if the acute mechanisms of glucose uptake at skeletal muscle, or the degree of augmentation will be the same in pregnancy, as the underlying cause is protective, compared to maladaptive in non-pregnant populations. Based on this, there is a gap in studies looking at both physiological mechanisms and clinical effects of acute exercise on glycaemic responses in pregnancy.

2.3.1 What dose of exercise is needed?

The metabolic response of the body to exercise is influenced by many factors, including the intensity, volume, duration, energy expenditure (total work) o, mode (weight-bearing or non-weight bearing; aerobic endurance or strength training under resistance load), carbohydrate consumption, and presence of chronic insulin resistance and abnormal glucose tolerance (Devlin et al., 1987). Acute and chronic exercise investigations that have compared the differential effects of exercise load-variables and modalities have produced a range of significant findings showing positive effects on acute blood glucose and insulin sensitivity, and longer-term glycaemic control. (Devlin, Hirshman et al. 1987, Chen, Stephens et al. 2003, Hansen, Dendale et al. 2009, Manders, Van Dijk et al. 2010, Roberts, Little et al. 2013, Krause, Rodrigues-Krause et al. 2014, Grace, Chan et al. 2017). Both exercise intensity and total energy expenditure have been described as key exercise variables for improving glycaemic control during exercise (Larsen, Dela et al. 1999, Grace, Chan et al. 2017). One area of rapidly growing research that has focused on manipulating these two variables is interval-based exercise. One advantage of this exercise structure is that by utilising short bouts of exercise with intermittent
rest (or active rest), participants can undertake exercise at higher intensities than they would likely be able to perform during continuous exercise. Depending on the protocol design, other practical benefits include reduced total volume of training and reduced training time, and depending on the population, with comparable or greater cardiometabolic training gains (Bartlett, Hwa Joo et al. 2012, Karstoft, Winding et al. 2014, Larsen, Welde et al. 2014, Mitranun, Deerochanawong et al. 2014).

2.3.2 Continuous or interval training for glycaemic control?

High intensity exercise/interval training (HIIT) has been the focus of much research in recent years, because of its potential for superior effects on cardiovascular and metabolic responses, and practical benefits for reducing other exercise variables, such as volume and duration. In healthy people, studies of HIIT, sprint interval training (SIT) and moderate intensity continuous training have produced comparable increases in the oxidative potential of skeletal muscle; a factor associated with insulin sensitivity (Gibala, Little et al. 2006, Burgomaster, Howarth et al. 2008, Hood, Little et al. 2011, Bartlett, Hwa Joo et al. 2012). In people with metabolic dysfunction, such as obesity and type 2 diabetes, evidence from HIIT and SIT studies has shown greater effects on glycaemic measures, including acute post-exercise blood glucose reduction, enhanced insulin signalling in skeletal muscle, and blunting post-prandial blood glucose levels over 24 hours, compared to traditional continuous training at moderate intensity (Tjonna, Lee et al. 2008, Karstoft, Winding et al. 2014, Mitranun, Deerochanawong et al. 2014). Thus, there is a growing volume of literature for the effectiveness of high intensity interval exercise. However, studies investigating changes in glycaemic responses to interval exercise when performed at intensities lower than high or supramaximal are scarce.

Interval training has only recently been explored in any context in pregnancy (Halse, Wallman et al. 2014, Ong, Wallman et al. 2016); however, there have been no investigations of the effects of an acute bout of interval structured exercise, compared with continuous exercise, on acute and 24-hour glycaemic responses in pregnant women. One study added 6 short bouts of self-paced higher intensity pedalling into a continuous cycling protocol, however the energy expenditure, as a product of total work, differed between the groups, and the protocol was not
distinct from a continuous protocol, to objectively compare effects on glucose responses (Ong, Wallman et al. 2016). While recent updates to the pregnancy guidelines now clearly advocate for moderate intensity exercise as the minimum standard, they also continue to recommend that pregnant women not currently exercising and/or who were inactive prior to pregnancy should commence exercise at a lower intensity level and for shorter duration (Hayman, Brown et al. 2016). This would mean that utilising a high intensity interval protocol at this stage would not align with available evidence or current pregnancy guidelines for women who are inactive. Based on this, and because the development of this study protocol and commencement of data collection began several years prior to the current guidelines being released, the present study has focused on a comparison of discontinuous exercise performed at moderate intensity with continuous exercise performed at low intensity.
CHAPTER THREE:

METHODS
3. METHODS

This study was approved by the University of Wollongong/Illawarra Shoalhaven Local Health District Health and Medical Human Research Ethics Committee (HE14/050, Appendix 1), with authorisation also approved by Illawarra Shoalhaven Local Health District Health Research Directorate (Appendix 2).

3.1 Participants

Pregnant and non-pregnant female volunteers were recruited for the investigation, with non-pregnant participants included to serve as a control group to identify whether potential changes in glycaemic and cardiometabolic responses to the different exercise protocols were also specific to pregnancy condition. All participants were aged between 18–40 years, non-smokers, and had no physical contraindications for exercise. Additional inclusion criteria for all pregnant participants were that they were in the second trimester (14–28 weeks) pregnancy, had completed at least the first antenatal consultation, confirmation of a singleton pregnancy, and absence of other associated risk factors for pre-term delivery (such as placenta previa, known high risk pregnancy or risk of uterus rupture). Additionally, participants with a fasting blood glucose level ≥5.1 mmol.L\(^{-1}\) (classification threshold for gestational diabetes\(^1\)) and early diagnosis of GDM in the pregnancy were included in the investigation. This is because the original study design involved three separate groups, being pregnant women, women with GDM and non-pregnant, healthy women (control). A combination to combine the GDM and the pregnancy women into one group and re-focus the study on pregnant women was due to significant recruitment challenges, and the raw blood glucose data

\(^1\) The Illawarra region of New South Wales (where the study was conducted) follows the Australian Diabetes in Pregnancy Society (ADIPS) guidelines for GDM testing and diagnosis, which includes an additional screening and diagnostic protocol for women identified as ‘at-risk’ for GDM conducted earlier than the traditional 24-28 weeks GDM screening. This is often in the first antenatal visit (Moses, Morris et al. 2011, Nankervis, McIntyre et al. 2013). Diagnosis is based on the threshold criteria recommended by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) from the results of the Hyperglycaemia and Adverse Pregnancy Outcome study (HAPO Study Cooperative Research Group 2008, International Association of Diabetes and Pregnancy Study Groups Consensus Panel 2010).
showing that all GDM women had baseline glycaemic responses within the clinically normal threshold for pregnancy (beyond their initial diagnostic level).

For non-pregnant participants, they were only controlled to match the age, non-smoking and no contraindications criteria. Other characteristics (previous pregnancy, phase of menstrual cycle, BMI, physical activity level) were not controlled, due to the pilot nature of this study.

3.1.1 Exercise Screening
Participants all completed a Physical Activity Readiness Questionnaire for Everyone, (PARQ+, Appendix 3), (Warburton, Gledhill et al. 2011). Pregnant participants underwent additional screening using the Physical Activity Readiness Medical Evaluation for Pregnancy (PARmed-X, Appendix 4), (Wolfe and Mottola, 2003). The PARmed-X was reviewed and signed by a medical practitioner or mid-wife. Screening processes were able to be completed during the first trimester for pregnant participants.

3.2 Experimental Procedures

3.2.1 Study Design
The study used a non-randomised design to compare individual responses over a 48-hour period (24-hours before exercise and 24-hours following exercise) to two different acute exercise protocols completed in consecutive phases (Figure 3.1). Participants first underwent a baseline submaximal exercise test (Phase 1), from which their individual workload (Watts) was calculated. This workload (watts) was then used for the Continuous exercise protocol (Phase 2). For the Discontinuous exercise protocol in Phase 3, the workload for exercise periods from Phase 2 was doubled and the actual exercise time was halved. While not ideal, the order of the exercise protocols was the same for all participants. The consecutive, non-randomised order was decided on to ensure that pregnant participants who were potentially inactive (during and/or prior to pregnancy), self-reported as ‘unfit’ and/or inexperienced with semi-recumbent cycling position, would first be able to complete the continuous protocol. This also ensured that the workload completed in the Continuous protocol directly informed the workload for the discontinuous protocol, meaning that total work (energy expenditure)
for each protocol was more accurately matched. The phases were completed over a minimum of three weeks and a maximum of six weeks, to limit the effects of physiological changes associated with progression of a normal pregnancy, in particular changes in hormone levels known to impact insulin sensitivity later in the second trimester (Catalano, Tyzbir et al. 1991, Catalano, Tyzbir et al. 1993, Sorenson and Brelje 1997). Between each phase, a minimum ‘washout’ period of 5 days was maintained. This was to ensure no carry-over of acute glycaemic effects from the previous exercise trial, no short-term training effects were observed from performing three repeated bouts of exercise in a short timeframe, and for practical consideration for participants who were required to adhere to standardisation elements for each phase, which included no purposeful exercise (other than the study protocol) for 24-hours prior to, and over the duration of each phase.

3.2.2 Acute exercise bout
A modified cycle ergometer (Lode BV Medical Technology; Excalibur Sport model; The Netherlands) was used to conduct the exercise protocols in each phase. Based on consultation with the University’s engineering department, the seat set-up for the ergometer was altered specifically for this study to be able to provide a broader saddle with back support in a semi-reclined seated posture (Figure 3.2 A and B). Semi-recumbent posture during cycling exercise in pregnant women has been shown to be safe and comparable to an upright (traditional) cycling posture, with similar maternal metabolic responses, including maternal and foetal heart rate responses (O’Neill, Cooper et al. 2006). The seat position, seat height and length to the pedals were modifiable and adjusted to suit each individual. These positions were recorded during Phase 1 to ensure replication for the subsequent trial phases. The Lode Excalibur model of cycle ergometer used enables workload (Watts) to be set and maintained, regardless of changes in individual pedal cadence. This allowed the workload for Phase 2 and Phase 3 to be set based on pre-determined watts, and not dependent on cadence. This addressed practical considerations for pregnant women at different stages of gestation comfort, size, and different experience levels with cycling exercise by removing the need for constant cadence.
Low and moderate aerobic exercise intensities have been utilised safely in healthy pregnant women, as well as among pregnant women with cardiovascular risk factors (obesity, physical inactivity), who have not exercised prior to or during pregnancy, and who have GDM or overt diabetes (Lesser, Gruppuso et al. 1996, Avery and Walker 2001, Coquart, Lemaire et al. 2008, Davenport, Charlesworth et al. 2008, Ong, Guelfi et al. 2009, Halse, Wallman et al. 2013). This component of the study design was determined (and implemented through commencement of data collection) prior to the current Australian guidelines release in 2016, where moderate intensity is recommended for all women (Hayman, Brown et al. 2016).

Figure 3.1 Study design
Figure 3.2: A) Participant set-up on the modified Lode ergometer B) Close up of modified seat-base, with rail and hydraulic system to permit changes to seat height, angle and length adjustment.
3.2.3 Study Protocol

3.2.3.1 Phase 1 – Study familiarisation and establishing individual workload

Phase 1 involved two components: (i) familiarisation with the laboratory, equipment and study protocol; (ii) a baseline exercise test. The components were completed either within the same session, or across two days, as chosen by each participant. Familiarisation involved demonstration of the continuous glucose monitoring device (CGM - Medtronic iPro2, MiniMed Inc. USA, depicted in Figure 3.3 A and B), and practice of self-testing BGL using the glucometer, or blood glucose monitor (ACCU-CHECK Performa, Roche Diagnostics 2013, depicted in Figure 3.3 C); trial of the oral-nasal respiratory face mask for correct size and fit; and detailed overview for exercise protocols and standardisation requirements for each phase, with further opportunity for questions. Participants were given a study diary to be used to record the timing and details of meals (including drinks), data for self-measured calibration BGL, medications, incidental physical activity, plus occurrence of other relevant events (i.e. stressful or emotional events, or an unusually physically intensive work day). Timing and values for calibration BGLs, meals, physical activity and medications were required for entry into the CGM database (Medtronic CareLink program) in order to accurately correlate glucose readings from the CGM device. Study diaries were also a back-up in the event of any significant anomalies in BGL data, to provide potential insight and identification of a reason for unexpected blood glucose responses.

Each participant was taken through the protocol for standardising meals to be the same for each day (24-hour period) in both phases. Participants developed their own individualised single-day meal plan (including accounting for drinks with caloric value) that they followed for each 24-hour period of the study in Phases 2 and 3. Those already following a prescribed dietary plan (e.g. GDM women) continued to use this for their study meal plan. Participants were encouraged to eat at the same or similar times wherever possible. This method for individual diet standardisation was designed in consultation with a dietitian experienced in pregnancy and gestational diabetes care, and has been previously used in healthy adults, type 2 diabetes and pregnant populations (Gibala, Little et al. 2006, Burgomaster, Howarth et al. 2008, Mikus, Oberlin et al. 2012, Halse, Wallman et al. 2013).
Baseline physical activity levels were identified during the familiarisation session. Questions were asked of each participant to determine current involvement in physical activity and exercise (covering type, regularity and volume per week, and estimated intensity based on qualitative description of exertion) in order to match against current Australian Physical Activity Guidelines. Pregnant participants were also asked about pre-pregnancy physical activity (over the preceding 12 months). The International Physical Activity Questionnaire was completed to identify a baseline of their normal weekly incidental activity (Craig, Marshall et al. 2003). Participants were encouraged to maintain similar incidental physical activity levels (e.g. walking with a pram between places or work-related tasks) during the study and were instructed to avoid any prolonged physical activity and not undertake additional exercise during the study phases. Walking or physical activity of 10 minutes duration or longer were recorded in the study diary. IPAQ responses were used to identify any substantial differences between Phases 2 and 3 in physical activity during the week prior to each phase. The commencement time of the exercise protocols was kept consistent across the phases for each individual to reduce potential BGL variation in relation to normal incidental activity, or meal times (pre-prandial or post-prandial exercise).

The baseline exercise test involved participants completing a sub-maximal cycle test on a modified Lode ergometer. Participants were set-up on the cycle ergometer for collection of metabolic expired gas (TrueOne® 2400, Parvo Medics, Utah USA), heart rate (Polar RS800CX monitor, paired with the Polar WearLink + transmitter W.LND sensor and strap - Polar Electro Oy, Finland), rating of perceived exertion (Borg 1982), capillary BGL via blood glucose monitor, and manual systolic and diastolic blood pressure (sphygmomanometer by Prestige Medical; stethoscope 3M™ Littman Classic II SE). Participants were rested for a 5-minute period seated on the ergometer before commencing a 2-minute warm-up at a low load (0-20 Watts). The test included three stages of 3-minute steady-stage cycling, with workload incrementally increased for each stage. Upon completion of the work periods, a 3-minute cool-down was performed at the same workload as the warm-up stage. Participants then rested for a 5-minute period on the ergometer.
Metabolic gas analysis was collected throughout the exercise protocol via using a two-way breathing, oral-nasal facemask (Face Mask Series 7910; Hans Rudolph Inc. USA), shown in Figure 3.2.2A. Heart rate (beats per minute, variability) were measured continuously, and blood pressure and perceived effort were measured in the third minute of each stage.

Following the cooldown and rest period, participants remained seated on the ergometer and attached to the metabolic cart. Predictive calculations of \( \dot{V}O_{2\text{peak}} \) using GraphPad Prism (Prism 6 for Windows, Version 6.07, June 2015, GraphPad Software, Inc.) were conducted:

\[
\text{Equation 1: Linear regression of Watts (X) and HR (Y), using aged-predicted maximum heart rate (HR}_{\text{max}} = 220\text{bpm} - [\text{age}]) = \text{prediction of peak exercise Watts.}
\]

\[
\text{Equation 2: Based on predicted peak Watts (equation 1), linear regression of Watts (X) and } \dot{V}O_2 \text{ response of each stage = predicted } \dot{V}O_{2\text{peak}}.
\]

From the predicted \( \dot{V}O_{2\text{peak}} \), the individual’s 25% \( \dot{V}O_{2\text{peak}} \) was calculated as the targeted oxygen consumption rate \( \dot{V}O_2 \) (L.min\(^{-1}\)) for the Continuous exercise protocol in Phase 2. To determine the Watts (workload) for the Continuous protocol, participants completed a short, 5-minute cycling trial to identify the workload on the ergometer with the targeted oxygen consumption rate \( \dot{V}O_2 \) (L.min\(^{-1}\)) on the metabolic cart.

### 3.2.3.2 Phases 2 and 3: Continuous and Discontinuous exercise protocols

Participants followed the same protocol over a 48-hour period, therefore Day 1 and Day 2 as described here were the same for Phase 2 and Phase 3. Participants attended the laboratory at the University of Wollongong (UOW) at their chosen start time of Day 1, which became their starting time for Day 1 and Day 2 (exercise trial) across both phases. Blood glucose was collected throughout the entire 48-hour period for each phase via CGM.

**Day 1 (Control) – no exercise**

Day 1 (24-hours) served as the control period with no exercise stimulus. Participants attended the laboratory. The IPAQ was completed, and the investigator also discussed any health changes since the previous session. The specific exercise protocol requirements were revised. A disposable sensor (Enlite\textsuperscript{TM} Glucose Sensor MMT-700A) was inserted subcutaneously at the
upper gluteal site via the compatible insertion device (Enlite\textsuperscript{TM} Serter, Medtronic MiniMed Inc. USA), as per the manufacturer’s instructions. An example of the insertion site and the monitor \textit{in-situ} on a participant is shown in Figure 3.3. This site was chosen to avoid any psychological aversion or barrier that pregnant participants may have had towards insertion at the abdominal site. The time of insertion was recorded.

Participants were required to take their BGL at 1-hour and 2-hour after the CGM was attached to activate and calibrate the device, as per the manufacturer’s instructions. The specific time points were recorded in Study Diary and added as mobile phone reminders, for reference.

A baseline BGL was measured and recorded manually by the investigator (capillary finger-prick testing with each participant’s allocated study glucometer). Participants were given a standardised snack - a small muesli bar (Carman’s Classic Fruit & Nut Muesli Bar – Bite Size, Carman’s Fine Foods, Victoria Australia; bite-sized portions purchased from Costco; but now discontinued at time of writing) containing 13 grams of carbohydrate (a single carbohydrate serve = 15 grams). Post-prandial BGL responses to the snack were manually measured at 5, 10, 15 and 30 minutes. The muesli bar was the only meal standardised across all participants in the study. With all other dietary components individualised to each participant, the inclusion of a standardised meal provided a valid method to evaluate acute post-prandial responses to different conditions, being exercise on Day 2 versus no exercise on Day 1; and Continuous exercise in Phase 2 versus Discontinuous exercise in Phase 3. Following the laboratory session, participants continued to follow their meal plan and record details of meals, regular BGL measures, medication and physical activity in the study diary.

\textit{Day 2 (Intervention) - acute exercise bout}

Day 2 (second 24-hours) served as the intervention day for Phase 2 and Phase 3. Participants attended the laboratory session at the same time as the previous day. The investigator asked about their general health on that day and reviewed the study diary to determine any difficulties or concerns with their monitored BGL and to ensure they were appropriate to continue with the exercise trial. The heart rate monitor was fitted, and participants were seated for 10 minutes, after which resting blood pressure, heart rate and baseline (pre-
exercise) BGL were measured. Participants were encouraged to have a drink of water prior to being set up on the ergometer.

Participants were seated on the ergometer, set up with oral-nasal facemask attached to the calibrated metabolic cart system and given time to ensure their set-up was comfortable. This time was also used to revise the specific exercise protocol procedures for the session. At the commencement of the trial, the starting time for the heart rate monitor, metabolic cart system and a separate stopwatch were all synced. Resting measures were then collected for 5 minutes while the participant was seated and stationary on the cycle ergometer, followed by a 2-minute warm-up on the ergometer with no load (0 Watts).

- **Continuous exercise (Phase 2):** 30-minutes continuous cycling at a load (watts) equivalent to low intensity, based on individual 25% predicted \( \dot{VO}_{2\text{peak}} \), calculated in Phase 1.
- **Discontinuous exercise (Phase 3):** total of 30-minutes discontinuous cycling, structured as 6 rounds of exercise and rest intervals, with equal interval duration of 2:30 minutes. This equated to 15 minutes of total exercise over the 30-minute protocol. Exercise intervals were performed at twice the Wattage used in Phase 2, aiming for approximately ~ 50% \( \dot{VO}_{2\text{peak}} \) prediction.

Heart rate was measured continuously throughout exercise via Polar RS800CX monitor (Polar Electro Oy, Finland), and manually recorded for participant monitoring every minute. Blood pressure was monitored every 5 minutes during the Continuous Protocol, and during the final minute of each interval of the Discontinuous Protocol. Similarly, RPE was recorded at the end of every 5 minutes of exercise during the Continuous Protocol and during the final 30 seconds of each work interval in the Discontinuous Protocol. Capillary BGL was manually measured by the investigator in the middle of each exercise protocol (at 12 \( \frac{1}{2} \) minutes, which fell during the third (of six) work intervals of the Discontinuous Protocol). Manual BGL was also measured immediately after the cessation of the 30-minute exercise period. After the exercise bout, participants remained seated for a 10-minute recovery period. The muesli bar snack was provided 15 minutes post-exercise, with BGLs collected at 5, 10, 15, 20, 25, 30- and 45-minutes.
On Day 3, at the completion of the 48 hours, the investigator removed the CGM device, and the completed study diary was collected from the participant.

### 3.3 Experimental Measurements

#### 3.3.1 Blood glucose

Blood glucose was collected throughout the entire 48-hour period for Phase 2 and Phase 3 via continuous glucose monitoring (CGM), as well as manually via glucometer prior to, during and for 30-minutes post-exercise. The use of CGM for measuring the effects of exercise interventions has been well demonstrated in type 2 diabetes, pregnancy and GDM studies, with no reported adverse events (Praet, Manders et al. 2006, Kestilä, Ekblad et al. 2007, McLachlan, Jenkins et al. 2007, Manders, Van Dijk et al. 2010, Dmitrovic, Katcher et al. 2011, Gillen, Little et al. 2012, Van Dijk, Manders et al. 2013). The iPro2 CGM device measures interstitial glucose by sampling every 5 minutes. It has a blinded interface, with BGL measured only provided retrospectively once data is downloaded to CareLink iPro Software online system. To calibrate the CGM device, participants were required to take a minimum of four manual BGL readings each day, including fasting and before bed to ensure the device’s calibration requirements were met. Participants with their own glucometer device (GDM women) continued to use their device. All other participants were provided with a glucometer device, disposable single-use lancets (ACCU-CHECK Safe-T-Pro Plus), testing strips (ACCU-CHEK Performa Test Strips), and a small disposable sharps container for used lancets and strips, shown in Figure 3.3. To reduce equipment or procedural differences on the reliability of BGL data, participants were fitted with the same CGM device and were given the same glucometer throughout the period of the investigation. The location and side of the body of CGM sensor insertion was recorded and then replicated for each phase. Participants were required to conduct their own BGL testing several times each day, so the method for finger-prick capillary testing was standardised, with the participants trained by the instructor to adopt an identical technique.
At the end of Day 3, the CGM device was removed and data were downloaded to Care Link iPro Software online system. Each woman was given a code to de-identify the data entry into the program. Details from the study diary were manually entered for calibration. The CGM device was cleaned thoroughly between each use, as per manufacturer’s instructions. The CareLink program settings for target blood glucose range were modified for the purpose of the study, with the high threshold set to 7.5 mmol.L\(^{-1}\) to align with the peak 1-hr post–prandial BGL target for pregnancy (Nankervis, McIntyre et al. 2013). The low threshold was kept at 3.9 mmol.L\(^{-1}\) as per the original settings of the device.

![Figure 3.3](image)

**Figure 3.3:** A) Continuous Glucose Monitor (CGM) sensor and device inserted at the upper gluteal subcutaneous site, B) CGM device covered by water-proof dressing to further secure position of device, C) Self-monitoring blood glucose equipment – disposable lancets, strips and glucometer.
3.3.1.1 Glycaemic control over 24-hours

Daily blood glucose control measures were calculated using the CGM data, and compared Day 1 (control day) and Day 2 (intervention day) for the following glycaemic measures (Rodbard 2012, Monnier, Colette et al. 2017):

- Mean BGL (mmol.L\(^{-1}\)) for the entire 24hr period; and the 8hrs overnight (10pm-6am)
- Standard deviation (standard deviation of BGL around the 24-hr mean BGL) (mmol.L\(^{-1}\)); also calculated for 8hrs overnight (10pm-6am)
- Coefficient of variation (%) of all BGL for the entire 24hr period (determined by \([\text{SD of glucose}] / \text{[mean glucose]}\])
- Minimum BGL (mmol.L\(^{-1}\)) recorded overnight (between 10pm-6am)

Fasting and post-prandial BGL responses during each 24-hour period were also compared:

- Fasting BGL (mmol.L\(^{-1}\)), presented as mean BGL (mmol.L\(^{-1}\)) over the 60 minutes prior to first meal or drink consumed; and peak BGL (mmol.L\(^{-1}\)) during 60 minutes prior to first meal or drink consumed
- Post-prandial (1-hour) BGL – the meal chosen for comparative measures of prolonged exercise effect on post-prandial BGL was selected as the main meal (breakfast, lunch, or dinner) that would correspond to 10–16 hours after exercise. Post-prandial measures are presented as i) mean BGL (mmol.L\(^{-1}\)) of three consecutive sample readings (representing a 15-minute window) identified at the 1-hour mark; and ii) peak post-prandial BGL within the first 60 minutes after eating.

3.3.1.2 Acute glycaemic responses post-exercise

As the CGM device had a blinded interface, BGL were also monitored manually by the investigator using the glucometer to allow appropriate management of participant BGL before, during and in recovery after exercise.

Using manual measures taken, baseline pre-exercise BGL was then compared to: i) immediate post-exercise BGL (mmol.L\(^{-1}\)) at the end of the exercise protocol; and ii) 15 minutes post-exercise BGL (mmol.L\(^{-1}\)).
The post-prandial BGL (1-hour after standardised snack) were analysed and compared using the CGM data. The use of 1-hour post-prandial is common as a clinical marker for glycaemic control in diabetes (Nankervis, McIntyre et al. 2013, Inzucchi, Bergenstal et al. 2015). Peak blood glucose level during the 60-minute postprandial timeframe was also compared between Day 1 and Day 2, as peak BGL was not expected to occur at the 1-hour post-prandial time point. Post-prandial BGL responses to the standardised snack were also manually measured by the investigator for 30 minutes (at 5, 10, 15 and 30 minutes), to be able to match the exact time points of the BGL’s obtained from the CGM data. Manual monitoring was kept to 30 minutes to reduce the total time required for participants to be in the laboratory.

3.3.2 Gas exchange

Measures of oxygen consumption ($\dot{V}O_2 \text{ L.min}^{-1}$), respiratory exchange ratio (RER), and minute ventilation ($\dot{V}E \text{ L.min}^{-1}$) were collected by TrueOne® 2400 metabolic cart. The system was calibrated before each use, following the manufacturer’s procedures using Alpha standard gas, and standardised volume syringe. Measurements were recorded every 15 seconds during pre-exercise baseline (5 minutes), exercise (30 minutes) and recovery (10 minutes) for each protocol. Raw data was downloaded to an excel file, where mean values for $\dot{V}O_2 \text{ L.min}^{-1}$, RER and $\dot{V}E$ during resting, exercising and recovery stages were calculated for each participant.

3.3.3 Cardiac frequency, heart rate variability and blood pressure

Heart rate was recorded via the Polar RS800CX monitor. Electrode cream was used to wet the electrode area of the strap to enhance conductivity during cycling. For each protocol, heart rate was continuously recorded during the rest (5 minutes), warm-up (2 minutes), exercise protocol (30 minutes) and recovery (10 minutes) stages.

Mean heart rate was measured for the following periods:

i. The 5-minute pre-exercise period: seated on ergometer attached to metabolic cart

ii. The entire 30-minute exercise protocol for each exercise intervention

iii. The 10-minute recovery period post-exercise intervention: participants remained seated on ergometer (with expired gas exchange collection also continuing).
Heart rate data was transferred from the Polar RS800CX via infrared Polar IRDA USB Adaptor Driver to a computer using Polar ProTrainer 5 software. Raw data was exported from Pro-Trainer into the Kubios HRV Analysis program for analysis (Version 2.2, May 2014; (Tarvainen, Niskanen et al. 2014)). Spectral analysis details include:

- Points in frequency-domain: 256 points/Hz
- FFT spectrum options: Window width 256 s, Window overlap 50 %
- AR spectrum options: AR model order 16, Use factorisation No

Heart rate variability data was collected and analysed from short-term (5-minute) recordings, and followed the European Society for Cardiology guidelines (Cardiology, Pacing et al. 1996). Within the Kubios analysis program, artefact correction was done to ‘very low’ or ‘low’ level correction only when there was a clearly identifiable signal disruption or occasional ectopic beat. This correction level was chosen as it was observed to remove outliers without over-correction of the rhythm. For an individual participant, the same correction level was used consistently for all of their analyses. Measures of HRV were collected in both the Time (Pnn50, SDNN, RMSSD, mean HR, mean RR) and Frequency (Peak Hz– Very Low Frequency VLF, Low Frequency LF, High Frequency LF; Absolute ms² – VLF, LF, HF, Total Power; Relative % - VLF, LF, HF; LF/HF ratio) domains. Frequency domain measures for absolute and peak spectral power were log transformed using a normal distribution and reported as normalised units (n.u.), based on the process recommended by European Society for Cardiology guidelines (Cardiology, Pacing et al. 1996).

The short-term (ST, 5-minute) sample recordings for both Time and Frequency measures were selected at a standardised time from the full HRV dataset of each protocol (resting, exercise, recovery period), as outlined below. If small adjustments in exact timing were required (based on signal disruption), the adjusted time was standardised across protocols for that participant:

- Resting: HR was recorded for 20 minutes in a stationary, semi-reclined position in a darkened and quiet room. The 5-minute sample was selected between minute-10 and
minute-15, or in the event of too much artefact, the nearest 5-minute period of continuous clean sampling.

- Exercise: This was a non-stationary sample. For the Continuous protocol, the 5-minute sample was selected between minute-15 and minute-20 during exercise. For the Discontinuous protocol, the 5-minute sample required 2 x 2½ minute consecutive exercise intervals to be combined using the Kubios software. This was done using either the 3rd and 4th exercise intervals, or 4th and 5th exercise intervals, based on the cleanest sample.

- Recovery: The 5-minute sample was selected from minute-3 until minute-7 of the 10-minute post-exercise recovery, which was in a stationary, seated position on the bike.

3.3.4 Psychophysical measures

3.3.4.1 Rating of perceived exertion

Rating of perceived exertion was measured via the Borg scale (Borg 1982), with participants providing a score from 6 (no exertion at all, or very, very light) to 20 (maximal exertion, or very, very hard). Participants were asked to first rate how hard the exercise felt for their whole body. They were then separately asked how to rate how hard the exercise felt specifically for their legs. This second rating was included based on the consideration that cycling is an isolated movement for the lower limbs, and for people not experienced with regular physical activity or the mode of cycling, their perception score of overall exertion might reflect localised leg muscular fatigue rather than whole body effort.

3.3.4.2 Qualitative perception of exercise difficulty and enjoyment

Adequate exercise participation for health benefit during pregnancy faces several perceptual and practical barriers for women (Duncombe, Wertheim et al. 2009, Evenson and Bradley 2010). Therefore, consideration is needed of not only whether a particular type of exercise is effective, but also whether it is acceptable and likely to be undertaken by pregnant women.
Two questions were asked at the completion of their study (end of Phase 3):

i) Reflecting on the experience of completing the two difference exercise trials, which of the 30 minutes did you find more difficult? Would you say ‘x’ protocol [the protocol identified as more difficult] was mildly, moderately or a lot more difficult? Were there any factors that you found made it more difficult?

ii) Reflecting on the experience of completing the two different exercise trials, which type of exercise did you find that you enjoyed more or would be more likely to choose to do as exercise? Was there any reason that you found ‘x’ protocol [the protocol identified as more enjoyable] more enjoyable?

3.4 Data analysis

A repeated measures two-way ANOVA, with post-hoc Tukey was performed to analyse the interactions between participant group and exercise protocol, and participant group and time (comparing pre-exercise 24hours to post-exercise 24-hours). For blood glucose changes post-exercise, metabolic gas exchange and HRV measures, the Time condition refers to pre-exercise (baseline), exercising and/or recovery periods. For 24-hour blood glucose measures (24 hour mean, standard deviation, coefficient of variation, fasting BGL, and post-prandial BGL), the Time condition refers to comparing Day 1 (no exercise) and Day 2 (after exercise).

A one-way ANOVA with Bonferroni pairwise comparisons were performed for pregnant women and non-pregnant women separately, to compare the specific effects of each protocol on acute blood glucose changes over time (pre-exercise, immediate post, 15 minutes post) following a single bout of exercise.

When the data for both groups was pooled to evaluate the effect of the protocol type (and removing pregnancy as a variable), a paired two-tailed t-test was used to analyse main effects.

Alpha was set at 0.05 for all analyses. All data has been reported as mean with 95% confidence intervals (CI), unless otherwise described as mean with standard deviation (SD).
CHAPTER FOUR:

RESULTS
4. RESULTS

4.1 Participants

4.1.1 Participant characteristics

Fourteen women completed all requirements of the study, with an equal number in the non-pregnant (n=7) and pregnant (n=7) groups. The baseline characteristics of the two groups are presented in Table 4.1. Mean age was not different between pregnant women and non-pregnant women. Mean BMI was also not significantly different. Four out of the seven pregnant women had been diagnosed with GDM early in their pregnancy, based on fasting levels ≥5.1mmo.l⁻¹.

Table 4.1 Participant baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>NON-PREGNANT</th>
<th>PREGNANT</th>
<th>Healthy</th>
<th>GDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.6 ± 6.6</td>
<td>31.9 ± 1.1</td>
<td>31.6</td>
<td>32</td>
</tr>
<tr>
<td>(22 - 39)</td>
<td>(30 - 37)</td>
<td>(31 - 37)</td>
<td>(30 - 33)</td>
<td></td>
</tr>
<tr>
<td>Gestation (week)</td>
<td>N/A</td>
<td>14 - 25</td>
<td>18 - 22</td>
<td>14 - 25</td>
</tr>
<tr>
<td>BMI (kg.m⁻²)</td>
<td>24.6 ± 2.7</td>
<td>26.1 ± 6.3</td>
<td>31</td>
<td>22.5</td>
</tr>
<tr>
<td>(18.9 - 27.3)</td>
<td>(20.9 - 37.5)</td>
<td>(22.8 - 37.2)</td>
<td>(20.9 - 24)</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td>n= 4</td>
<td>n= 3</td>
<td>n= 0</td>
<td>n= 3</td>
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<tr>
<td>guidelines met</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous pregnancy</td>
<td>n= 2</td>
<td>n= 6</td>
<td>n= 3</td>
<td>n= 3</td>
</tr>
<tr>
<td>Prior GDM</td>
<td>n= 1</td>
<td>n= 0</td>
<td>n= 0</td>
<td>n= 0</td>
</tr>
<tr>
<td>Medical conditions</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Asthma (n= 2)</td>
<td>Hypothyroid (n= 2)</td>
<td>Hypothyroid (n= 1)</td>
<td>Hypothyroid (n= 1)</td>
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</tr>
<tr>
<td>Inflammatory Bowel</td>
<td>Coccyx nerve pain (n= 1)</td>
<td>Coccyx nerve pain (n= 1)</td>
<td>Coccyx nerve pain (n= 1)</td>
<td></td>
</tr>
<tr>
<td>Syndrome (n= 1)</td>
<td>Depression (n= 1)</td>
<td>Depression (n= 1)</td>
<td>Depression (n= 1)</td>
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</tr>
<tr>
<td>Depression (n= 1)</td>
<td>Scoliosis (n= 1)</td>
<td>Scoliosis (n= 1)</td>
<td>Scoliosis (n= 1)</td>
<td></td>
</tr>
<tr>
<td>Complications in</td>
<td>Pre-eclampsia (n= 1)</td>
<td>Pre-eclampsia (n= 1)</td>
<td>Pre-eclampsia (n= 1)</td>
<td></td>
</tr>
<tr>
<td>previous pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Non-Pregnant (n =7), Pregnant (n =7) with a sub-grouping of Normoglycaemia (n = 3) and Gestational Diabetes Mellitus (GDM, n = 4). Age, Gestation and Body Mass Index (BMI) are presented as the mean and range. All other values show incidence.
4.1.2 Adverse events

No participants had low baseline blood glucose levels that required an intake of carbohydrate prior to commencing exercise during any phase of the study. Furthermore, no blood glucose levels either during or post-exercise were observed below 4.0 mmol.L⁻¹. There were no reported episodes or symptoms of hypoglycaemia during or post-exercise, nor throughout the full duration of any participant’s trials. The downloaded data from CGM did identify blood glucose readings indicative of low blood sugar (<3.5 mmol.L⁻¹) for several individuals during overnight recordings. These low overnight readings occurred in participants in both groups (and were not only those with GDM), did not occur repeatedly in the same individual, and were not associated with any symptoms or adverse outcomes.

Two participants (non-pregnant) experienced a brief episode of light-headedness during one insertion of the CGM. Both were rested in a supported seated posture in a chair in the laboratory and monitored for 10-minutes. Their blood pressures were within normal ranges, and no further signs or symptoms followed. One pregnant participant reported symptoms of light-headedness towards the end of the recovery phase of one trial (continuous exercise). This had been anticipated due to her measured low blood pressure during Phase 1, which she reported as normal based on similar experiences in her previous pregnancy. The participant was able to complete the recovery phase seated on the ergometer and was then assisted in moving to a supported chair, where blood pressure and heart rate monitoring continued, and water was provided until reported symptoms had subsided, and blood pressure and heart rate readings were within the resting range. No other adverse events or abnormal responses were observed or reported during baseline, exercise or recovery monitoring periods throughout the study.
4.2 Glycaemic control

4.2.1 Baseline – Day 1

No difference (p= 0.37) in baseline mean 24-hour blood glucose (BGL) was observed between pregnant women (5.26 mmol.L\(^{-1}\) (CI 4.99, 5.54), and non-pregnant women (5.42 mmol.L\(^{-1}\) (CI 5.18, 5.66). Similarly, no difference (p= 0.56) was observed in overnight BGL (5.07 mmol.L\(^{-1}\) (CI 4.64, 5.50) and 4.89 mmol.L\(^{-1}\) (CI 4.52, 5.26), and fasting BGL (p= 0.98), (5.29 mmol.L\(^{-1}\) (CI 4.93, 5.64) and 5.29 mmol.L\(^{-1}\) (CI 5.01, 5.57) between pregnant and non-pregnant women, respectively. In comparison to reference values for optimal glycaemic target levels, both groups had relatively normal glycaemic control.

4.2.2 Exercise - acute blood glucose responses

A significant interaction (protocol x time) between protocol type (Continuous versus Discontinuous) and time (pre-exercise, immediately post-exercise, and 15 minutes post-exercise) on acute changes in BGL was observed in both pregnant (p= 0.020) and non-pregnant (p= 0.008) group (presented in Table 4.2).

The effects of continuous and discontinuous exercise were analysed for each participant group to determine their effect on acute blood glucose changes over time (between pre-exercise, immediate post-exercise, and 15 min post-exercise, presented in Table 4.2). In pregnant women, the reduction in blood glucose showed a significant interaction over time for both Continuous (F (2,12) = 5.476; p= 0.020) and Discontinuous exercise (F (2,12) = 7.838; p= 0.008). This has been presented in Figure 4.1. Post-hoc analysis showed that there was a trend towards significance for reduction in blood glucose from baseline to the time-point immediately post-exercise within both protocols (continuous: F (2,12) = 5.476 p= 0.067) and discontinuous: (F (2,12) = 7.838, p=0.059). Acute BGL was reduced by 10.1% following discontinuous exercise from 5.67 mmol.L\(^{-1}\)(SD 0.47) to 5.1 mmol.L\(^{-1}\) (SD 0.62) (p= 0.008), and by 4.9% following continuous exercise, from 5.24 mmol.L\(^{-1}\) (SD 0.42) to 4.99 mmol.L\(^{-1}\) (p= 0.020).

For non-pregnant women, the interaction over time was significant for Continuous exercise (F (2,12) = 6.492, p= 0.012), but not for Discontinuous exercise (F (2,12) = 2.024, p=0.175) for BGL.
changes across baseline, immediate post-exercise and 15 minutes post-exercise time points (Figure 4.1). However, post-hoc analysis in the non-pregnant group did not show any significance (or trend close to significance) for BGL reduction following either protocol for any specific time point (immediate or 15 minutes post-exercise). Figure 4.1 depicts a similar pattern of acute BGL reduction observed in pregnant and non-pregnant women for the Continuous protocol; however, the blood glucose changes for the Discontinuous exercise in non-pregnant women do not follow the same pattern as observed in pregnant women.

The 1-hour post-prandial BGL in response to a standard snack is presented in Table 4.3. No interaction \((protocol \times time)\) was observed on post-prandial BGL responses between Day 1 (no exercise) and Day 2 (following exercise, with snack consumed 15 minutes post-exercise) in either pregnant or non-pregnant women (Table 4.3).

However, when participant groups were pooled to compare direct effects of the exercise protocols only, there was a significantly lower 1-hr post prandial BGL following exercise on Day 2 for both protocols, compared to Day 1. This data is presented in Table 4.4.

### 4.2.3 Exercise – 24-hour glycaemic control

Mean, standard deviation and coefficient of variation results for 24-hour blood glucose data (following each exercise protocol) are presented in Table 4.3. No significant interaction \((group \times time)\) for either exercise protocol was observed in mean 24-hour blood glucose before and after exercise. Similarly, there was no differences observed in measures of 24-hour variability of blood glucose levels after exercise, when compared to variability observed in baseline 24-hr BGL. Two other clinical measures of glucose control, fasting BGL and post-prandial (1-hour) BGL for a meal that was consumed more than 10 hours after the exercise bout were also not influenced by maternal status over time (Table 4.3). Therefore, for exercise protocol and maternal status, no significant change in blood glucose level, blood glucose variability, be it fasting or post-meal state, were observed in the 24-hour post-exercise period.
However, when participant groups were pooled to analyse the overall effect of the two different exercise protocols on acute blood glucose responses, there were significant differences observed. Pooled data comparing the effects of continuous and discontinuous exercise protocols on all blood glucose measures is presented in Table 4.4. Discontinuous exercise significantly increased mean 24-hr blood glucose level, however, this effect was not observed for the continuous protocol. Exercise also significantly modified BGL 24-hr variability. Continuous exercise significantly lowered the standard deviation of 24-hr BGL by 16.68%, from 0.74 mmol.L\(^{-1}\) (CI 0.60, 0.88) on Day 1 to 0.62 mmol.L\(^{-1}\) (CI 0.43, 0.80) on Day 2. Following Discontinuous exercise (p= 0.002), 24-hour BGL standard deviation was also reduced significantly from 0.7609 mmol.L\(^{-1}\) (CI 0.6332, 0.8885) on Day 1 (exercise) to 0.53 mmol.L\(^{-1}\) (CI 0.46, 0.60) on Day 2, a 19.06% reduction. The coefficient of variation for 24-hour BGL was significantly reduced in the Discontinuous exercise condition only, lowered by 33.51% from Day 1 (14.28% (CI 11.26, 17.30) to Day 2 (9.39% (CI 8.30, 10.49). Additionally, only Discontinuous exercise was associated with a significant increase in overnight mean BGL but a significant reduction in the overnight BGL variability. Interestingly, when compared to the minimum BGL measured overnight on Day 1 (prior to exercise), higher overnight minimum BGL were observed following exercise for both Continuous and Discontinuous exercise protocols (Table 4.3).
### Table 4.2 Acute blood glucose responses to exercise

<table>
<thead>
<tr>
<th>Acute Exercise BGL changes (mmol.L(^{-1}))</th>
<th>Pre-exercise</th>
<th>Immediate post</th>
<th>15-min post</th>
<th>One-way ANOVA</th>
<th>Bonferroni multiple comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>5.24</td>
<td>4.99</td>
<td>4.99</td>
<td>(P=0.02) F (2, 12) = 5.48</td>
<td>(P=0.67 (-0.19, 0.53))</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>5.67</td>
<td>5.10</td>
<td>5.40</td>
<td>(P=0.008) F (2, 12) = 4.48</td>
<td>(P=0.59 (-0.23, 1.17))</td>
</tr>
<tr>
<td>Non-pregnant women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>5.56</td>
<td>5.13</td>
<td>5.16</td>
<td>(P=0.012) F (2, 12) = 6.49</td>
<td>(P=0.14 (-0.14, 1.05))</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>5.60</td>
<td>5.31</td>
<td>5.40</td>
<td>(P=0.18) F (2, 12) = 2.02</td>
<td>(P=0.26 (-0.17, 0.74))</td>
</tr>
</tbody>
</table>

Note: Data presented was analysed one-way ANOVA, with Bonferroni multiple comparisons and \(P\leq0.05\).

Non-Pregnant (n = 7), Pregnant (n = 7), with all measures presented as mean, 95% confidence intervals (CI).
Table 4.3 Glycaemic measures over time in response to exercise, relative to pregnancy condition and protocol type.

<table>
<thead>
<tr>
<th>GLYCAEMIC MEASURE</th>
<th>PROTOCOL</th>
<th>PREGNANT</th>
<th>NOT PREGNANT</th>
<th>Pregnancy x time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1 - control</td>
<td>Day 2 - intervention</td>
<td>Day 1 - control</td>
<td>Day 2 - intervention</td>
</tr>
<tr>
<td>24-HOUR BGL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24hr mean (mmol.L(^{-1}))</td>
<td>Continuous</td>
<td>5.21</td>
<td>4.75, 5.68</td>
<td>5.30</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>5.32</td>
<td>4.87, 5.76</td>
<td>5.39</td>
</tr>
<tr>
<td>24hr SD (mmol.L(^{-1}))</td>
<td>Continuous</td>
<td>0.58</td>
<td>0.49, 0.68</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>0.70</td>
<td>0.50, 1.06</td>
<td>0.51</td>
</tr>
<tr>
<td>24hr CV (%)</td>
<td>Continuous</td>
<td>11.24</td>
<td>9.41, 13.06</td>
<td>9.35</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>14.96</td>
<td>8.43, 21.49</td>
<td>9.18</td>
</tr>
<tr>
<td>Overnight mean (mmol.L(^{-1}))</td>
<td>Continuous</td>
<td>5.00</td>
<td>4.31, 5.69</td>
<td>5.31</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>5.14</td>
<td>4.41, 5.87</td>
<td>5.40</td>
</tr>
<tr>
<td>Overnight SD (mmol.L(^{-1}))</td>
<td>Continuous</td>
<td>0.34</td>
<td>0.25, 0.43</td>
<td>0.32</td>
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<tr>
<td></td>
<td>Discontinuous</td>
<td>0.43</td>
<td>0.29, 0.62</td>
<td>0.32</td>
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<tr>
<td>Overnight minimum (mmol.L(^{-1}))</td>
<td>Continuous</td>
<td>4.27</td>
<td>3.61, 4.93</td>
<td>4.73</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>4.33</td>
<td>3.40, 5.26</td>
<td>4.99</td>
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</table>

ACUTE BGL RESPONSES

<table>
<thead>
<tr>
<th></th>
<th>Exercise protocol x time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting – 1hr mean (mmol.L(^{-1}))</td>
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</tr>
<tr>
<td>Continuous</td>
<td>5.30</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>5.27</td>
</tr>
<tr>
<td>Fasting – peak (mmol.L(^{-1}))</td>
<td>Pregnant</td>
</tr>
<tr>
<td>Continuous</td>
<td>5.61</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>5.67</td>
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<tr>
<td>1hr post prandial – mean (mmol.L(^{-1}))</td>
<td>Pregnant</td>
</tr>
<tr>
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<td>6.30</td>
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<tr>
<td>Discontinuous</td>
<td>6.16</td>
</tr>
<tr>
<td>1-hr post prandial – mean (mmol.L(^{-1}))</td>
<td>Main meal</td>
</tr>
<tr>
<td>Continuous</td>
<td>5.74</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>6.07</td>
</tr>
<tr>
<td>1-hr post prandial – peak (mmol.L(^{-1}))</td>
<td>Main meal</td>
</tr>
<tr>
<td>Continuous</td>
<td>5.87</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>6.77</td>
</tr>
</tbody>
</table>

Note: Data presented was analysed by two-way ANOVA (repeated measures) with post-hoc Tukey and P < 0.05. Non-Pregnant (n = 7), Pregnant (n = 7), with all measures presented as mean, 95% confidence intervals (CI).
Table 4.4 Comparison of Continuous and Discontinuous exercise on glycaemic measures in all participants.

<table>
<thead>
<tr>
<th>GLYCAEMIC MEASURE</th>
<th>CONTINUOUS EXERCISE</th>
<th>DISCONTINUOUS EXERCISE</th>
<th>Pooled Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1 - control</td>
<td>Day 2 - intervention</td>
<td>Day 1 - control</td>
</tr>
<tr>
<td></td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
</tr>
<tr>
<td>24-HOUR BGL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24hr mean (mmol.L⁻¹)</td>
<td>5.29 5.00, 5.58</td>
<td>5.44 5.26, 5.63</td>
<td>5.39 0.40, 0.11 5.64 5.47, 5.82</td>
</tr>
<tr>
<td>24hr SD (mmol.L⁻¹)</td>
<td>0.74 0.60, 0.88</td>
<td>0.62 0.43, 0.80</td>
<td>0.76 0.63, 0.89 0.53 0.46, 0.60</td>
</tr>
<tr>
<td>24hr CV (%)</td>
<td>14.10 11.27, 16.92</td>
<td>11.93 8.28, 15.57</td>
<td>14.28 11.26, 17.30 9.39 8.30, 10.49</td>
</tr>
<tr>
<td>Overnight mean (mmol.L⁻¹)</td>
<td>4.92 4.49, 5.34</td>
<td>5.23 4.90, 5.56</td>
<td>5.04 4.66, 5.42 5.43 5.22, 5.64</td>
</tr>
<tr>
<td>Overnight SD (mmol.L⁻¹)</td>
<td>0.42 0.33, 0.49</td>
<td>0.407 0.25, 0.57</td>
<td>0.44 0.36, 0.53 0.31 0.23, 0.38</td>
</tr>
<tr>
<td>Overnight minimum (mmol.L⁻¹)</td>
<td>4.05 3.52, 4.58</td>
<td>4.64 4.33, 4.95</td>
<td>4.24 3.79, 4.68 4.99 4.78, 5.19</td>
</tr>
</tbody>
</table>

**ACUTE BGL RESPONSES**

<table>
<thead>
<tr>
<th></th>
<th>Fasting – 1hr mean (mmol.L⁻¹)</th>
<th>Fasting – peak (mmol.L⁻¹)</th>
<th>1-hr post prandial – mean (mmol.L⁻¹)</th>
<th>1-hr post prandial – peak (mmol.L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.25 4.90, 5.60</td>
<td>5.07 4.73, 5.41</td>
<td>5.33 5.04, 5.62</td>
<td>5.40 5.21, 5.58</td>
</tr>
<tr>
<td></td>
<td>5.56 5.22, 5.91</td>
<td>5.31 4.95, 5.68</td>
<td>5.69 5.45, 5.92</td>
<td>5.57 5.37, 5.77</td>
</tr>
<tr>
<td>1-hr post prandial – mean (mmol.L⁻¹)</td>
<td>6.65 6.29, 7.01</td>
<td>5.52 5.14, 5.91</td>
<td>6.56 6.14, 6.98</td>
<td>5.85 5.52, 6.18</td>
</tr>
<tr>
<td>1-hr post prandial – peak (mmol.L⁻¹)</td>
<td>6.02 5.43, 6.61</td>
<td>6.04 5.65, 6.43</td>
<td>6.52 6.00, 7.05</td>
<td>6.54 6.08, 6.99</td>
</tr>
<tr>
<td>1-hr post prandial – peak (mmol.L⁻¹)</td>
<td>6.33 5.65, 7.00</td>
<td>6.62 6.22, 7.02</td>
<td>6.84 6.32, 7.35</td>
<td>6.47 6.00, 6.95</td>
</tr>
</tbody>
</table>

Note: Data presented was analysed by Paired t-tests (two-tailed), with significance of P <0.05.

Pregnant and non-pregnant women were pooled (n = 14), with all measures reported as mean, with 95% confidence intervals (CI).
Figure 4.1 * indicates significant change (p <0.05).
Acute blood glucose changes are shown from baseline pre-exercise to immediate post-exercise and 15-minute post-exercise, presented as mean (central line) and 95% confidence intervals (bars). Pregnant women (top graph) had a significant interaction over time, measured by one-way ANOVA for both Continuous (p= 0.020) and Discontinuous (p= 0.008) exercise, showing a reduction in blood glucose. Non-pregnant women (bottom graph) had a significant interaction for Continuous exercise only (p= 0.012).
4.3 Metabolic gas exchange measures

4.3.1 Baseline (pre-exercise) gas exchange

No significant interactions between pregnancy and exercise protocol (group x protocol) were observed for any resting metabolic measures (Figure 4.2, Table 4.5). When just the resting period prior to each protocol was examined, there was no significant difference in resting $\dot{VO}_2$ between pregnant women and non-pregnant women prior to the Continuous protocol or the Discontinuous protocol (Figure 4.2). Respiratory exchange ratio (RER) prior to the Continuous protocol also did not differ at rest between pregnant women and non-pregnant women. However, prior to the Discontinuous protocol, RER was significantly higher in the pregnant group compared to non-pregnant. Resting minute ventilation ($\dot{V}_E$) before the Continuous protocol was higher in the pregnant group compared to non-pregnant women and similarly before the Discontinuous protocol a significant difference was found between pregnant women and non-pregnant women.

When participants were pooled to permit specific comparison between the protocols only, there was no difference in resting $\dot{VO}_2$, RER or $\dot{V}_E$ due to exercise protocol (Table 4.6).

4.3.2 Exercising gas exchange

Overall, exercising oxygen consumption was not significantly different between the two exercise protocols (Figure 4.2). No interaction ($p=0.648$, group x protocol) was found between pregnancy condition and the protocol type. Mean $\dot{VO}_2$ was 0.768 L.min$^{-1}$ (CI 0.621, 0.915) during Continuous exercise and 0.738 L.min$^{-1}$ (CI 0.583, 0.893) during Discontinuous exercise. This demonstrated that the total metabolic work completed by participants was equivalent. A representative example of this for an individual participant is shown in Figure 4.3. Furthermore, it reflects that any differences in the physiological responses to the two protocols are more likely attributed to the effect of exercise intensity (low vs. moderate), structure (Continuous vs. Discontinuous), or the combination of both, rather than the metabolic work of the exercise. No interaction (group x protocol) was observed for RER or $\dot{V}_E$ (Table 4.5).
When participants were pooled (presented in Table 4.6), the $\dot{V}O_2$ for each exercise protocol remained similar ($p= 0.373$), with Continuous $\dot{V}O_2$ (0.747 L.min$^{-1}$ (CI 0.651, 0.843) and Discontinuous $\dot{V}O_2$ (0.728 L.min$^{-1}$ (CI 0.635, 0.820). RER was observed to be significantly higher ($p< 0.0001$) during Discontinuous exercise compared to Continuous exercise. No difference was observed for $\dot{V}E$ between the two exercise protocols among pooled participants.

4.3.3 Acute recovery gas exchange

There were no significant interactions between pregnancy condition and type of exercise (protocol) for recovery $\dot{V}O_2$ (Figure 4.2), RER or $\dot{V}E$ (presented in Table 4.5).

When participants were pooled, there were no significant differences in the effects of discontinuous vs. continuous exercise for any recovery metabolic measures (presented in Table 4.6). However, differences were found when comparing recovery to the baseline period prior to exercise. For Continuous exercise, post-exercise $\dot{V}O_2$ (or excess post-exercise oxygen consumption, EPOC) was significantly higher during recovery than at baseline. For Discontinuous exercise, the difference was not significant between resting level and recovery level. Similarly, following continuous exercise, recovery minute ventilation ($\dot{V}E$) was significantly higher than the baseline measure. Yet the difference was not significant for Discontinuous exercise. In contrast, both Continuous and Discontinuous protocols had a significantly higher RER during recovery compared to baseline RER.
Table 4.5: Effects of Continuous and Discontinuous exercise on metabolic responses during rest, exercise and recovery, relative to pregnancy condition

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>Rest</th>
<th>Exercise</th>
<th>Recovery</th>
<th>Rest</th>
<th>Exercise</th>
<th>Recovery</th>
<th>Pregnancy x Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td></td>
</tr>
<tr>
<td>RER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>0.89</td>
<td>0.92</td>
<td>0.90</td>
<td>0.85</td>
<td>0.88</td>
<td>0.87</td>
<td>P=0.54 F (1, 12) = 0.40</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>0.91</td>
<td>1.01</td>
<td>0.98</td>
<td>0.84</td>
<td>0.94</td>
<td>0.86</td>
<td>P=0.44 F (1, 12) = 0.63</td>
</tr>
<tr>
<td>VE (L.min⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>11.63</td>
<td>26.44</td>
<td>12.91</td>
<td>9.06</td>
<td>21.49</td>
<td>8.57</td>
<td>P=0.43 F (1, 12) = 0.68</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>11.92</td>
<td>26.45</td>
<td>13.39</td>
<td>9.10</td>
<td>17.68</td>
<td>8.61</td>
<td>P=0.78 F (1, 12) = 0.01</td>
</tr>
<tr>
<td>RPE – All (6-20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>- -</td>
<td>9.6</td>
<td>8.83</td>
<td>- -</td>
<td>8.71</td>
<td>7.24</td>
<td>P=0.65 F (1, 12) = 0.22</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>- -</td>
<td>10.8</td>
<td>9.38</td>
<td>- -</td>
<td>9.59</td>
<td>8.02</td>
<td>- -</td>
</tr>
<tr>
<td>RPE – Legs (6-20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>- -</td>
<td>9.7</td>
<td>7.98</td>
<td>- -</td>
<td>8.69</td>
<td>7.32</td>
<td>P=0.11 F (1, 12) = 3.04</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>- -</td>
<td>11.6</td>
<td>9.50</td>
<td>- -</td>
<td>9.97</td>
<td>8.48</td>
<td>- -</td>
</tr>
</tbody>
</table>

Note: Data presented was analysed by two-way ANOVA (repeated measures), with P<0.05.
Non-Pregnant (n = 7), Pregnant (n = 7), with all measures presented as mean, 95% confidence intervals (CI).
Rest = 5 min pre-exercise (REST), exercise = 30-min exercise bout (EX), recovery =10 min post-exercise (REC), RPE = rating of perceived exertion (6-20 scale).
Table 4.6 Comparison of Continuous and Discontinuous exercise on metabolic responses, with pregnant and non-pregnant women pooled (n= 14)

<table>
<thead>
<tr>
<th>Metabolic responses</th>
<th>Rest</th>
<th>Exercise</th>
<th>Recovery</th>
<th>Pooled Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V02 (L.min⁻¹)</td>
<td>0.27</td>
<td>0.24</td>
<td>0.30</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.07</td>
<td>0.03</td>
<td>0.05</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>0.35</td>
<td>0.26</td>
<td>0.27</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td><strong>P= 0.91</strong></td>
<td><strong>t=0.12 df=13</strong></td>
<td><strong>t=0.37 df=13</strong></td>
<td><strong>t=0.37 df=13</strong></td>
</tr>
<tr>
<td><strong>DISCONTINUOUS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V02 (L.min⁻¹)</td>
<td>0.27</td>
<td>0.26</td>
<td>0.35</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>0.07</td>
<td>0.04</td>
<td>0.06</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>0.35</td>
<td>0.26</td>
<td>0.27</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td><strong>P= 0.37</strong></td>
<td><strong>t=0.92 df=13</strong></td>
<td><strong>t=0.71 df=13</strong></td>
<td><strong>t=0.71 df=13</strong></td>
</tr>
<tr>
<td>RER</td>
<td>0.87</td>
<td>0.84</td>
<td>0.89</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>0.90</td>
<td>0.87</td>
<td>0.89</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>0.90</td>
<td>0.87</td>
<td>0.89</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td><strong>P= 0.0001</strong></td>
<td><strong>t=6.21 df=13</strong></td>
<td><strong>t=0.88 df=13</strong></td>
<td><strong>t=0.88 df=13</strong></td>
</tr>
<tr>
<td>VE (L.min⁻¹)</td>
<td>10.34</td>
<td>9.24</td>
<td>11.45</td>
<td>10.51</td>
</tr>
<tr>
<td></td>
<td>23.97</td>
<td>26.80</td>
<td>26.80</td>
<td>26.79</td>
</tr>
<tr>
<td></td>
<td>21.13</td>
<td>12.07</td>
<td>13.54</td>
<td>12.29</td>
</tr>
<tr>
<td></td>
<td><strong>P= 0.68</strong></td>
<td><strong>P= 0.93</strong></td>
<td><strong>P= 0.10</strong></td>
<td></td>
</tr>
</tbody>
</table>

Note: Data presented was analysed by Paired t-tests (two-tailed), with significance of P<0.05. All measures are reported as mean, with 95% confidence intervals (CI). Pregnant and non-pregnant women were pooled (n= 14).

Rest = 5 min pre-exercise (REST), exercise = 30-min exercise bout (EX), recovery =10-min post-exercise (REC).
Figure 4.2 This graph shows the mean oxygen consumption levels (with 95% confidence interval bars) at rest, during exercise (30 min Ex) and during recovery. There was no significant difference observed between pregnant and non-pregnant women, for either protocol.

Figure 4.3 Representative data from one participant depicts comparable oxygen consumption (VO\textsubscript{2} L.min\textsuperscript{-1}) and heart rate (HR, beats per min) between the two different exercise protocols.
4.4 Heart rate variability

4.4.1 Resting HRV measures

At baseline, there were significant differences between pregnant and non-pregnant women observed for several resting HRV measures (Table 4.7). Time-domain measures of pNN50 (p=0.0388) and RMSSD (p=0.0304) were significantly higher at rest in the non-pregnant group (pNN50 (27.46% (CI 4.488, 50.44), RMSSD (50.39 ms (CI 25.15, 75.63) compared to the pregnant group (pNN50 (1.91% (CI -1.037, 4.859), RMSSD (16.10 ms (CI 8.793, 23.40). The high frequency (HF) spectral component, measured as absolute power and presented in normalised units, was also significantly higher (p= 0.0353) among non-pregnant women (6.444 n.u (CI 5.259, 7.629) than pregnant women (4.407 n.u (CI 3.456, 5.358). No further differences in the resting frequency-domain measures between groups were found. Mean heart rate at rest was higher (p= 0.0204) in pregnant participants at 86.37 bpm (CI 78.62, 94.12) than non-pregnant participants at 69.28 bpm (CI 61.56, 76.99). The mean interval between QRS complexes (mean R-R) was significantly shorter (p= 0.0158) in pregnant women at 701.8 ms (CI 641.2, 762.3) compared to non-pregnant women at 881.2 ms (CI 792.1, 970.4).

Table 4.7 Time and Frequency domain HRV measures at rest in pregnant and non-pregnant women.

<table>
<thead>
<tr>
<th>HRV MEASURE</th>
<th>PREGNANT</th>
<th>NOT PREGNANT</th>
<th>P =</th>
<th>t (df=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>86.3</td>
<td>78.6, 94.1</td>
<td><strong>P= 0.02</strong></td>
<td>(t=3.13, df=6)</td>
</tr>
<tr>
<td>R-R interval (ms)</td>
<td>701.8</td>
<td>641.2, 762.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>1.91</td>
<td>-1.04, 4.99</td>
<td><strong>P= 0.04</strong></td>
<td>(t=2.63, df=6)</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>16.10</td>
<td>8.79, 23.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>32.80</td>
<td>17.52, 48.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF peak (n.u)</td>
<td>-2.74</td>
<td>-2.99, -2.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF absolute (n.u)</td>
<td>5.55</td>
<td>4.56, 6.54</td>
<td><strong>P= 0.20</strong></td>
<td>(t=1.445, df=6)</td>
</tr>
<tr>
<td>LF relative (%)</td>
<td>33.96</td>
<td>25.25, 42.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF peak (n.u)</td>
<td>-1.35</td>
<td>-1.66, -1.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF absolute (n.u)</td>
<td>4.41</td>
<td>3.46, 5.36</td>
<td><strong>P= 0.035</strong></td>
<td>(t=2.71, df=6)</td>
</tr>
<tr>
<td>HF relative (%)</td>
<td>12.34</td>
<td>4.82, 19.86</td>
<td><strong>P= 0.14</strong></td>
<td>(t=1.71, df=6)</td>
</tr>
<tr>
<td>LF/HF</td>
<td>3.85</td>
<td>1.54, 6.17</td>
<td><strong>P= 0.14</strong></td>
<td>(t=1.72, df=6)</td>
</tr>
<tr>
<td>TP 5 min (ms)</td>
<td>6.67</td>
<td>5.84, 7.50</td>
<td><strong>P= 0.07</strong></td>
<td>(t=2.20, df=6)</td>
</tr>
<tr>
<td>VLF peak (n.u)</td>
<td>-4.94</td>
<td>-5.72, -4.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLF absolute (n.u)</td>
<td>6.03</td>
<td>5.21, 6.85</td>
<td><strong>P= 0.09</strong></td>
<td>(t=2.01, df=6)</td>
</tr>
<tr>
<td>VLF relative (%)</td>
<td>53.67</td>
<td>43.27, 64.07</td>
<td><strong>P= 0.44</strong></td>
<td>(t=0.82, df=6)</td>
</tr>
</tbody>
</table>

Note: Data presented was analysed by Paired t-tests (two-tailed), with significance of P<0.05. 
Non-Pregnant (n = 7), Pregnant (n = 7). All measures are reported as mean, with 95% confidence intervals (CI).
4.4.2 Exercising responses due to protocol

A significant interaction (group x protocol) was observed for the RMSSD Time Domain measure (p= 0.02) between pregnancy and type of exercise during a single bout of exercise. During Continuous exercise, RMSSD in non-pregnant women was 38.1% higher at 15.15ms (CI 9.08, 21.21) compared to pregnant women at 9.39 ms (CI 0.85, 17.92). In contrast, RMSSD during Discontinuous exercise was 25.2% higher in pregnant women at 12.31 ms (CI -1.61, 26.24) than the non-pregnant women at 9.21 ms (5.78, 12.64), however there were no post-hoc differences found. No other interactions (group x protocol) were found for time-domain measures during acute exercise (Table 4.8). For Frequency Domain measures, there was a significant interaction (group x protocol) in the low frequency (LF) spectral component (p = 0.03). During Continuous exercise, LF (absolute power) was 30.6% greater in non-pregnant women (5.06 n.u (CI 4.53, 5.61) than pregnant women (3.15 n.u (CI 2.03, 5.00). This interaction remained significant with post-hoc comparisons. However, during Discontinuous exercise, LF (absolute power) was 5.9 % greater in pregnant women (5.50 n.u (CI 4.22, 6.77) than in non-pregnant women (5.17 n.u (CI 4.45, 5.89). There was no post-hoc differences found for discontinuous exercise. No other interactions (group x protocol) were observed for frequency-domain measures during acute exercise (Table 4.8).

When participant groups were pooled to allow a specific comparison of only the exercise protocol responses, SDNN was significantly higher (p= 0.01) during Discontinuous exercise than during Continuous exercise. However, no other time domain variables were found to be significantly different between the two protocols. This data is presented in Table 4.9. Significant differences were also observed with respect to the frequency domain. The LF absolute power measure was significantly greater (p< 0.0001) during Discontinuous exercise compared to Continuous exercise. In contrast, both peak LF and relative LF were significantly greater (p< 0.0001 and p= 0.0073 respectively) during Continuous exercise than during Discontinuous exercise. The HF relative power was also higher (p= 0.0018) during the Continuous exercise compared to Discontinuous exercise, while the LF/HF ratio was greater (p= 0.0267) in Discontinuous exercise compared to Continuous exercise. However, neither peak HF nor absolute HF were significantly different between the exercise protocols (Table 4.9).
4.4.3 Acute recovery responses

No significant interactions (group x protocol) were found between pregnancy condition and protocol type for any time-domain or frequency domain measures during the recovery period (captured between minute-3 and minute-7-following exercise (Table 4.8).

When participants were pooled, there was no significant difference in any HRV measures during recovery between Continuous and Discontinuous exercise (Table 4.9).
Table 4.8  Heart rate variability responses with exercise, related to pregnancy and type of exercise protocol performed.

<table>
<thead>
<tr>
<th>HRV MEASURE</th>
<th>PROTOCOL</th>
<th>PREGNANT</th>
<th>NOT PREGNANT</th>
<th>Pregnancy x protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time domain</td>
<td>Exercise</td>
<td>Recovery</td>
<td>Exercise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
<td>Mean + 95% CI</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>Continuous</td>
<td>113.0 99.9, 126</td>
<td>90.7 76.5, 104.8</td>
<td>96.7 88.4, 105.3</td>
</tr>
<tr>
<td>R-R interval (ms)</td>
<td>Continuous</td>
<td>538.6 479, 598.2</td>
<td>754.9 500.9, 1009</td>
<td>575.4 455.3, 695.5</td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>Discontinuous</td>
<td>0.85 -1.23, 2.93</td>
<td>6.08 -0.67, 12.84</td>
<td>0.89 0.05, 1.73</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>Continuous</td>
<td>9.39 0.85, 17.92</td>
<td>23.65 6.79, 40.51</td>
<td>15.15 9.08, 21.21</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>Discontinuous</td>
<td>12.31 -1.61, 26.24</td>
<td>24.70 -3.51, 52.91</td>
<td>9.21 5.78, 12.64</td>
</tr>
<tr>
<td>Frequency domain</td>
<td>Continuous</td>
<td>-2.50 -2.68, -2.32</td>
<td>-2.64 -3.00, -2.29</td>
<td>-2.58 -2.90, -2.25</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>-2.98 -3.10, -2.86</td>
<td>-2.92 -3.15, -2.68</td>
<td>-3.00 -3.15, -2.85</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>3.52 2.03, 5.00</td>
<td>6.93 4.55, 9.31</td>
<td>5.06 4.52, 5.61</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>5.50 4.22, 7.87</td>
<td>5.24 3.77, 6.72</td>
<td>5.17 4.45, 5.89</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>33.04 20.16, 45.92</td>
<td>34.31 20.37, 48.26</td>
<td>39.47 27.08, 51.87</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>23.95 11.19, 36.71</td>
<td>26.83 14.97, 36.94</td>
<td>17.83 10.57, 25.10</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>-1.55 -1.92, -1.17</td>
<td>-1.54 -1.75, -1.32</td>
<td>-1.39 -1.75, -1.02</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>-1.83 -1.94, -1.71</td>
<td>-1.49 -1.79, -1.20</td>
<td>-1.48 -1.77, -1.19</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>2.58 0.72, 4.44</td>
<td>6.02 3.43, 8.61</td>
<td>4.05 3.15, 4.95</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>3.72 2.58, 4.86</td>
<td>4.56 3.04, 6.09</td>
<td>3.91 3.36, 4.46</td>
</tr>
<tr>
<td>LF peak (n.u.)</td>
<td>Continuous</td>
<td>16.00 4.14, 27.86</td>
<td>15.17 6.60, 23.74</td>
<td>14.44 9.43, 19.45</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>4.06 2.24, 5.88</td>
<td>16.04 3.62, 28.46</td>
<td>5.80 0.19, 11.40</td>
</tr>
<tr>
<td>HF absolute (n.u.)</td>
<td>Continuous</td>
<td>1.77 1.39, 2.16</td>
<td>0.68 -0.04, 1.40</td>
<td>1.01 0.59, 1.43</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>4.74 3.62, 5.85</td>
<td>8.12 5.37, 10.87</td>
<td>6.04 5.34, 6.74</td>
</tr>
<tr>
<td>LF/HF</td>
<td>Continuous</td>
<td>7.04 5.84, 8.23</td>
<td>6.68 5.53, 7.83</td>
<td>7.08 6.12, 8.04</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>-4.76 -5.51, -4.02</td>
<td>-5.05 -5.66, -4.44</td>
<td>-3.48 -5.02, -1.95</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>-4.84 -5.17, -4.50</td>
<td>-4.57 -5.35, -3.80</td>
<td>-4.93 -5.25, -4.62</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>3.98 3.08, 4.88</td>
<td>7.36 4.37, 10.34</td>
<td>5.21 4.28, 6.15</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>6.69 5.45, 7.92</td>
<td>6.06 5.04, 7.08</td>
<td>6.81 5.74, 7.88</td>
</tr>
<tr>
<td></td>
<td>Discontinuous</td>
<td>50.89 30.17, 71.61</td>
<td>50.45 30.05, 70.86</td>
<td>45.95 32.94, 58.97</td>
</tr>
<tr>
<td></td>
<td>Continuous</td>
<td>71.97 58.08, 85.85</td>
<td>56.99 38.65, 75.32</td>
<td>76.35 64.92, 87.79</td>
</tr>
</tbody>
</table>
Note: Data presented was analysed by two-way ANOVA (repeated measures), with P<0.05. Non-Pregnant (n = 7), Pregnant (n = 7), with all measures presented as mean, 95% confidence intervals (CI).

Non-Pregnant and non-pregnant women were pooled (n= 14). All measures are reported as mean, with 95% confidence intervals (CI).

From previous page Table 4.8
Note: Pooled data presented was analysed by Paired t-tests (two-tailed), with significance of P<0.05.

Table 4.9 Heart rate variability during Continuous vs. Discontinuous exercise, with participant groups pooled.

<table>
<thead>
<tr>
<th>HRV MEASURE</th>
<th>CONTINUOUS</th>
<th></th>
<th></th>
<th>DISCONTINUOUS</th>
<th></th>
<th></th>
<th></th>
<th>Pooled Data</th>
<th></th>
<th></th>
<th></th>
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<td></td>
<td>EXERCISE</td>
<td>RECOVERY</td>
<td></td>
<td>EXERCISE</td>
<td>RECOVERY</td>
<td></td>
<td></td>
<td>EXERCISE</td>
<td>RECOVERY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>104.8</td>
<td>96.6, 113.0</td>
<td>83.9</td>
<td>75.1, 92.7</td>
<td>115.4</td>
<td>105.5, 125.4</td>
<td>88.1</td>
<td>79.8, 96.3</td>
<td>P= 0.01</td>
<td>t=3.01</td>
<td>df=13</td>
</tr>
<tr>
<td>R-R interval (ms)</td>
<td>582.2</td>
<td>540.1, 624.2</td>
<td>777.4</td>
<td>658.5, 896.2</td>
<td>537.6</td>
<td>477.7, 597.5</td>
<td>704.5</td>
<td>630.1, 779.0</td>
<td>P= 0.07</td>
<td>t=1.99</td>
<td>df=13</td>
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<tr>
<td>pNN50 (%)</td>
<td>0.87</td>
<td>-0.08, 1.82</td>
<td>13.06</td>
<td>4.310, 21.80</td>
<td>1.12</td>
<td>-0.37, 2.61</td>
<td>12.47</td>
<td>1.867, 23.07</td>
<td>P= 0.49</td>
<td>t=0.72</td>
<td>df=13</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>12.27</td>
<td>7.50, 17.03</td>
<td>31.32</td>
<td>19.69, 42.95</td>
<td>10.76</td>
<td>4.61, 16.91</td>
<td>37.23</td>
<td>16.11, 58.35</td>
<td>P= 0.43</td>
<td>t=0.81</td>
<td>df=13</td>
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<tr>
<td>SDNN (ms)</td>
<td>18.39</td>
<td>13.70, 23.08</td>
<td>49.00</td>
<td>34.83, 63.17</td>
<td>44.60</td>
<td>24.04, 65.15</td>
<td>51.50</td>
<td>34.26, 68.73</td>
<td>P= 0.01</td>
<td>t=3.01</td>
<td>df=13</td>
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<tr>
<td>Frequency domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF peak (n.u)</td>
<td>-2.54</td>
<td>-2.70, -2.38</td>
<td>-2.68</td>
<td>-2.87, -2.50</td>
<td>-2.99</td>
<td>-3.07, -2.91</td>
<td>-2.72</td>
<td>-2.91, -2.53</td>
<td>P&lt; 0.0001</td>
<td>t=5.69</td>
<td>df=13</td>
</tr>
<tr>
<td>LF absolute (n.u)</td>
<td>4.60</td>
<td>3.93, 5.26</td>
<td>6.80</td>
<td>5.71, 7.89</td>
<td>6.75</td>
<td>6.05, 7.44</td>
<td>6.21</td>
<td>5.31, 7.11</td>
<td>P&lt; 0.0001</td>
<td>t=6.30</td>
<td>df=13</td>
</tr>
<tr>
<td>LF relative (%)</td>
<td>36.26</td>
<td>28.43, 44.08</td>
<td>34.21</td>
<td>27.08, 41.34</td>
<td>20.89</td>
<td>14.40, 27.38</td>
<td>33.34</td>
<td>24.02, 42.66</td>
<td>P= 0.0073</td>
<td>t=3.18</td>
<td>df=13</td>
</tr>
<tr>
<td>HF peak (n.u)</td>
<td>-1.47</td>
<td>-1.69, -1.24</td>
<td>-1.51</td>
<td>-1.65, -1.37</td>
<td>-1.65</td>
<td>-1.82, -1.48</td>
<td>-1.54</td>
<td>-1.70, -1.37</td>
<td>P= 0.13</td>
<td>t=1.62</td>
<td>df=13</td>
</tr>
<tr>
<td>HF absolute (n.u)</td>
<td>3.32</td>
<td>2.34, 4.30</td>
<td>6.08</td>
<td>4.86, 7.30</td>
<td>3.82</td>
<td>3.28, 4.36</td>
<td>5.57</td>
<td>4.59, 6.55</td>
<td>P= 0.28</td>
<td>t=1.14</td>
<td>df=13</td>
</tr>
<tr>
<td>HF relative (%)</td>
<td>15.22</td>
<td>9.74, 20.70</td>
<td>18.75</td>
<td>12.63, 24.86</td>
<td>4.93</td>
<td>2.38, 7.48</td>
<td>19.47</td>
<td>11.52, 27.43</td>
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<td>t=3.90</td>
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</tr>
<tr>
<td>LF/HF</td>
<td>3.04</td>
<td>2.12, 3.96</td>
<td>2.57</td>
<td>1.47, 3.66</td>
<td>5.25</td>
<td>3.76, 6.74</td>
<td>2.43</td>
<td>1.56, 3.29</td>
<td>P= 0.03</td>
<td>t=2.50</td>
<td>df=13</td>
</tr>
<tr>
<td>TP 5 min (ms)</td>
<td>5.39</td>
<td>4.71, 6.07</td>
<td>7.95</td>
<td>6.72, 9.19</td>
<td>7.06</td>
<td>6.41, 7.71</td>
<td>7.43</td>
<td>6.73, 8.14</td>
<td>P= 0.0003</td>
<td>t=4.92</td>
<td>df=13</td>
</tr>
<tr>
<td>VLF peak (n.u)</td>
<td>-4.12</td>
<td>-4.94, -3.31</td>
<td>-4.73</td>
<td>-5.19, -4.27</td>
<td>-4.89</td>
<td>-5.08, -4.69</td>
<td>-4.51</td>
<td>-4.97, -4.06</td>
<td>P= 0.08</td>
<td>t=1.92</td>
<td>df=13</td>
</tr>
<tr>
<td>VLF absolute (n.u)</td>
<td>4.29</td>
<td>3.47, 5.11</td>
<td>7.14</td>
<td>5.82, 8.47</td>
<td>5.33</td>
<td>4.71, 5.96</td>
<td>6.60</td>
<td>6.04, 7.17</td>
<td>P= 0.04</td>
<td>t=2.32</td>
<td>df=13</td>
</tr>
<tr>
<td>VLF relative (%)</td>
<td>48.42</td>
<td>37.94, 58.90</td>
<td>47.00</td>
<td>36.99, 57.01</td>
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<td>66.42, 81.90</td>
<td>47.09</td>
<td>35.93, 58.25</td>
<td>P= 0.0008</td>
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<td>df=13</td>
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</tbody>
</table>

Note: Pooled data presented was analysed by Paired t-tests (two-tailed), with significance of P<0.05.
4.5 Psychophysical measures

The rating of perceived exertion during exercise (RPE) was not affected by pregnancy, with no interaction observed between group and type of protocol (presented in Table 4.5).

When participant groups were pooled, RPE scores for total effort (10.19 (CI 9.225, 11.16) and for leg effort (10.78 (CI 9.588, 11.97) were both significant higher (p= 0.006 and p= 0.0005 respectively) during the Discontinuous protocol than the Continuous protocol (9.171 (CI 8.410, 9.933) total body, and 9.214 (CI 8.217, 10.21) - for legs).

Qualitative data from participants’ subjective reporting on their perception of the relative difficulty of the two protocols was more varied. Four participants (3 pregnant, 1 non-pregnant) reported that the Discontinuous protocol ‘felt moderately more difficult’, and described this as being related to noticing a higher body temperature and changes in their heart rate; four women reported the Discontinuous protocol as being ‘slightly more difficult’ than continuous (3 non-pregnant, 1 pregnant), while a further four reported perceiving no difference in the difficulty between the two protocols (3 non-pregnant, 1 pregnant). The remaining two participants reported that the Continuous protocol was ‘moderately more difficult’. Both of these women were in the pregnancy group and described that they perceived breathing effort and overall fatigue levels to be greater by the continuous effort without rest.

When asked which of the two exercise protocols they found more enjoyable, the majority of participants (12/14) reported that they enjoyed the exercise experience of performing the Discontinuous protocol more than the Continuous protocol. The reasons provided ranged from enjoyment of working harder, feeling confident to work harder, and finding it more physically comfortable to have rest breaks between exercising (the latter was only identified by pregnant participants). For the two people who reported enjoying the Continuous protocol more, both described this as related to finding the heavier workload on their legs during the discontinuous protocol challenging, and both reported that they had not ridden a bike ‘for a while’.
CHAPTER FIVE:

DISCUSSION
5.0 DISCUSSION

This investigation found there was a difference in the acute blood glucose responses to the two exercise protocols over time in pregnant versus non-pregnant women. In pregnant women, 15 minutes of moderate intensity, discontinuous cycling and 30 minutes of low intensity continuous cycling both had the effect of significantly reducing blood glucose from pre-exercise baseline level to immediate post-exercise and remained at 15-minutes post-exercise. In non-pregnant women, however, acute reductions in blood glucose were only found with the Continuous protocol. For all other measures of daily glycaemic control, there were no significant effects found for either protocol in either group.

With both groups identified as having normal daily blood glucose levels throughout the study period, the data for pregnant and non-pregnant women were combined to allow a direct comparison of the effects of two exercise protocols, without the primary variable of pregnancy. When pooled, a bout of moderate intensity, discontinuous exercise resulted in different changes to 24-hour glycaemic control compared low intensity, continuous cycling of matched total work. Following the discontinuous protocol, the mean 24-hour blood glucose level significantly increased but remained within the normal clinical range; while daily blood glucose variability measures (standard deviation of BGL around the 24-hr mean; coefficient of variation of glucose) were significantly reduced. Following the continuous protocol, however, there were no significant effects on mean 24-hour blood glucose. Standard deviation of 24-hour blood glucose was significantly lowered, but there was no significant change to the coefficient of variation. Thus, changes observed in 24-hour glycaemic control was influenced by the intensity and structure of the preceding acute exercise bout. This suggests that, independent of total work (energy expenditure), glycaemic control over 24-hour may be able to be augmented through the intensity of exercise undertaken. The differences in 24-hour glycaemic measures in response to the two exercise protocols may also have been related to potential changes substrate utilisation and sympathetic/parasympathetic balance, with respect to changes in metabolic gas exchange and heart rate variability measures observed during discontinuous exercise and within the recovery period.
5.1 Acute changes with exercise

5.1.1 Blood glucose changes in pregnant women

Acute exercise-related blood glucose responses in pregnant women have been linked to the exercise intensity and duration (Artal, Platt et al. 1981, Bonen, Campagna et al. 1992, Davenport, Mottola et al. 2008, Ruchat, Davenport et al. 2012). Fifteen minutes of light treadmill walking in the third trimester has been shown to maintain blood glucose levels (Artal, Platt et al. 1981). However, moderate exercise intensity for a 30-minute period resulted in blood glucose declining by approximately 25% in the second trimester, and 31% in the third trimester. The non-pregnant control group recording only a 15% reduction over the same bout of exercise (Bonen, Campagna et al. 1992). The present study demonstrated that a bout of discontinuous exercise at moderate intensity and a bout of continuous exercise at lower intensity produced different results for blood glucose changes over time, when undertaken by pregnant women compared with non-pregnant women. This difference occurred despite the continuous and discontinuous exercise protocols being matched for total work (energy expenditure). Importantly, for pregnant women both types of exercise had positive effects on acutely reducing blood glucose. This was not the case for non-pregnant women, where only continuous exercise led to significant blood glucose reductions in the short term (15-minutes post-exercise). The responses observed in pregnant women following 30 minutes of light intensity exercise showed that a reduction of acute blood glucose could be achieved at a lower intensity than previously reported by Bonen, Campagna et al. (1992). Furthermore, exercise performed in a discontinuous structure at moderate intensity, which only involved a total of 15 minutes of work (and 15 minutes of rest) also led to significant reduction of acute blood glucose. Artal, Platt et al. (1981) found no change in blood glucose following 15-minutes of continuous, light exercise. Thus, the observations of the present study support that for exercise bouts of shorter duration, intensity is likely an important variable for inducing acute glycaemic changes in pregnant women.

Despite this study being a pilot study, it was interesting to observe that in just this small cohort of pregnant women (n = 7) with blood glucose measures within the normal ranges, both continuous and discontinuous protocols were able to result in positive reductions of acute blood glucose levels. Given that large individual variations in blood glucose levels are normal, a larger sample
size and ability to include participants with blood glucose levels above the normal ranges would have been more effective at showing acute and 24-hour blood glucose changes in both pregnant and non-pregnant women. Irrespective of the continuity of the exercise protocol, this investigation observed a significant reduction in acute blood glucose levels in pregnant women at exercise intensities and duration (of work) that were lower than that previously reported (Artal, Platt et al. 1981, Bonen, Campagna et al. 1992).

Greater blood glucose reductions following acute exercise in pregnant women compared to non-pregnant have been previously attributed to alterations in the pathways of glycogenolysis and gluconeogenesis in pregnancy (Lotgering, Spinnewijn et al. 1998, Bessinger, McMurray et al. 2002). A recent study reported that after 20 minutes of steady-state exercise (vigorous intensity), similar rates of plasma glucose reduction were observed for pregnant (34-38 weeks) and non-pregnant women, matched for physical activity background, while after 40 minutes, glucose concentrations in non-pregnant women had significantly increased but were almost unchanged in pregnant women (Mottola, Inglis et al. 2013). The current study also observed that continuous exercise had similar effects for reducing blood glucose in pregnant and non-pregnant women. Yet, there were differences between the two groups following the discontinuous exercise, with a significant effect found for pregnant women only. As pregnancy is a condition of progressive insulin resistance, it is associated with higher levels of circulating insulin (Bonen, Campagna et al. 1992, Bessinger, McMurray et al. 2002). Bonen, Campagna et al. (1992) suggested that while pregnancy-related insulin resistance was acutely reduced by exercise (via the effect of exercise-enhanced insulin sensitivity), overall insulin levels present during exercise in pregnant women remained higher than those of non-pregnant women. Indeed, Mottola, Inglis et al. (2013) also reported plasma insulin to be twice as high in pregnant compared to non-pregnant women throughout the exercise bout. Early research shows insulin to be inhibitory to glycogenolysis, and potentially to gluconeogenesis (Felig and Wahren 1971), meaning that higher circulating insulin levels in pregnant women may contribute to the impaired or delayed hepatic glucose production in response to glycogen depletion, as suggested by Bessinger, McMurray et al. (2003). Thus, the differences observed in the present study between pregnant women and non-pregnant women may relate to enhanced glucose uptake stimulated by exercise, but also to altered hepatic glucose
production in response to glycogen depletion of exercise. Furthermore, a higher level of circulating insulin during exercise in pregnant women (compared to non-pregnant) would allow for a greater degree of exercise stimulated insulin-dependent mechanisms of glucose uptake.

With respect to exercise intensity and pregnancy, a study of acute exercise effects in women with gestational diabetes found that moderate-intensity exercise had a greater effect on reducing acute blood glucose levels compared to low intensity exercise (Avery and Walker 2001). The current study is not directly comparable as the participants were found to have normal blood glucose levels over the course of the study, despite the pregnancy group including women with diagnosed GDM, or with risk factors for abnormal glucose tolerance (high BMI pre-pregnancy, inactive). However, in the current study, both discontinuous and continuous exercise protocols had similar effects on reducing acute post-exercise blood glucose in pregnant women. Novel differences in the current study were the discontinuous structure of the moderate intensity bout, which mean only 15 minutes of total exercise were undertaken to elicit blood glucose reductions (compared to 30-minutes in the earlier study), and the matched total work (energy expenditure) between protocols. Previous studies in type 2 diabetes have suggested that energy expenditure is the key variable for post-exercise effects on blood glucose (Larsen, Dela et al. 1999). As total work was not controlled in the Avery and Walker study (2001), the reductions in blood glucose observed post-exercise may have not been related only to exercise intensity but also to differences in energy expenditure between the two exercise trials. Both trials were performed for 30 minutes, and at a relatively higher intensity than the current study.

When total work is controlled, it has been observed that low (40%VO_{2peak}) and high (80%VO_{2peak}) intensity bouts of exercise both led to similar increases in skeletal muscle GLUT4 mRNA and GLUT4 protein in healthy individuals (Kraniou, Cameron-Smith et al. 2006). As the primary glucose transporter protein for skeletal muscle tissue, similar increases in GLUT4 synthesis would have likely increased both insulin-mediated and contraction-driven glucose uptake during exercise (Zisman, Peroni et al. 2000, Kraniou, Cameron-Smith et al. 2006). In the current study, the total work output performed was equal for the discontinuous and continuous exercise; therefore, post-exercise blood glucose changes were not attributable to obvious differences in
exercise energy expenditure between the protocols. Rather, overall energy expenditure may have been lower than required to elicit significant and sustained blood glucose reductions in short-term post-exercise period.

In the current study, participants from both the pregnant group (3 out of 7) and the non-pregnant group (5 out of 7) were classified as above the healthy weight range by BMI (pre-pregnancy). BMI itself was not significantly different between groups (26.14 kg.m\(^{-2}\) compared to 24.63 kg.m\(^{-2}\) respectively); however, the standard deviation of the pregnancy group (SD 6.31), with two participants categorised as obese or morbidly obese, was more than double that of the non-pregnant group (SD 2.749). Perhaps unexpectedly, the GDM women in the pregnancy group were all within healthy weight range according to BMI classification. Both groups also had similar baseline blood glucose levels, which (other than the fasting levels for GDM), were within clinical target ranges of optimal glycaemic control (Inzucchi, Bergenstal et al. 2012, Nankervis, McIntyre et al. 2013). Therefore, having women with an obese BMI prior to pregnancy, as well as women with GDM in the pregnant group means this group may represent higher underlying levels of skeletal muscle insulin resistance and glycaemic dysfunction than would be normally associated with general pregnancy (Leturque, Burnol et al. 1984, Kuhl 1991, Sorenson and Brelje 1997, Barbour, McCurdy et al. 2007, Colomiere, Permezel et al. 2010). Nevertheless, it is still clinically important that there were significant effects of both exercise protocols on post-exercise blood glucose levels in this pregnant group.

5.1.2 Metabolic exercise response
The current study found no interaction between maternal status and exercise protocol (continuous vs. discontinuous) on exercise oxygen consumption. This result supports previous studies, where no difference was observed in submaximal oxygen consumption between pregnant and non-pregnant women, suggesting that pregnancy alone does not significantly increase metabolic demands during mild or moderate intensity exercise (Guzman and Caplan 1970, Lotgering, Gilbert et al. 1985, Sady, Carpenter et al. 1989, Jaque-Fortunato, Wiswell et al. 1996, Avery, Wolfe et al. 2001). Metabolic demands increase with progressing gestation during weight-bearing exercise (e.g. treadmill walking), but remains relatively unaffected by pregnancy
during weight-supported modes, for example cycling, where metabolic demand is independent of body weight (Artal, Masaki et al. 1990, Carpenter, Sady et al. 1990, Pivarnik, Lee et al. 1991). In the current study where cycling was the selected exercise mode, gestational stage of pregnant participants did vary from the start to the end of the second trimester, yet there was no difference in exercising oxygen consumption, relative to maternal condition. Therefore, the results support the previous studies discussed earlier that the exercise mode of semi-recumbent cycling does not affect exercising metabolic demands differently for pregnant women compared with non-pregnant women and offers a practical exercise choice for women to engage in regular or daily exercise while avoiding the weight-bearing effects of higher metabolic costs of exercise with progressive gestation.

Similarly, no interactions were observed in the exercising minute ventilation between exercise protocol and pregnancy status. This finding is in line with earlier research showing that minute ventilation during exercise was not different in pregnant participants compared to non-pregnant controls (Lotgering, Spinnewijn et al. 1998, Avery, Wolfe et al. 2001), but contrasts an earlier study that reported minute ventilation as significantly higher during submaximal exercise in pregnant women compared to non-pregnant women (Jaque-Fortunato, Wiswell et al. 1996). There was also no interaction observed in the respiratory exchange ratio between exercise protocol and pregnancy status. As a relative measure of fat compared to carbohydrate substrate utilisation, the finding of a similar exercising respiratory exchange ratio between pregnant and non-pregnant women suggests that substrate utilisation did not differ between the two protocols relative to pregnancy condition. This supports earlier literature that found no difference in respiratory exchange ratio during exercise in pregnancy, compared to non-pregnant condition (Jaque-Fortunato, Wiswell et al. 1996, Bessinger, McMurray et al. 2002).

As there was no interaction between pregnancy status and exercise protocol type on oxygen consumption, respiratory exchange ratio or minute ventilation, the data of pregnant and non-pregnant participants were combined to enable a direct comparison between the continuous and discontinuous protocols, without the primary variable of pregnancy. From this, there was no significant difference in exercising oxygen consumption found between the exercise protocols,
which showed that total work (representing exercise energy expenditure) was shown to be well controlled and equal between the protocols; a planned outcome of the adopted research design. The pooled analysis found a significantly higher respiratory exchange ratio during discontinuous exercise compared to continuous exercise, which reflects greater carbohydrate substrate utilisation during the discontinuous bout. A recent study also demonstrated significantly greater respiratory exchange ratio in the immediate post-exercise recovery (0 - 5 minutes) following 10 minutes of high intensity interval training compared with 30 minutes of moderate intensity, continuous cycling (Metcalf, Koumanov et al. 2015). In the current study, the exercise intensity was significantly lower than has been researched in traditional high intensity interval training. Furthermore, the work to rest intervals of 2 ½ minutes used in the current investigation were longer than well-established high intensity interval protocols that usually incorporate intervals of one minute or less (Gibala, Little et al. 2006, Burgomaster, Howarth et al. 2008, Gillen, Little et al. 2012). Intervals of moderate intensity were chosen to be appropriate for pregnant women not regularly exercising, or with a background of cardiometabolic risks including physical inactivity, obesity and gestational diabetes mellitus (Davenport, Charlesworth et al. 2008, Hayman, Brown et al. 2016). Despite the relatively lower intensity compared to the existing literature, the combination of discontinuous periods of moderate intensity exercise used in the present study was enough to elicit a significant shift from baseline (towards higher carbohydrate metabolism).

5.1.3 Sympathetic and parasympathetic modulation during exercise
Metabolic dysfunction that occurs with obesity and diabetes is associated with increased sympathetic activity and reduced heart rate variability (HRV) (Singh, Larson et al. 2000, Maser, Lenhard et al. 2014). Healthy pregnancy without any glycaemic dysfunction (beyond the natural biological progression in insulin resistance with advancing gestation) is also associated with changes in autonomic control, with a shift towards relatively greater sympathetic modulation and lower parasympathetic control at rest (Ekholm, Hartiala et al. 1997, Maser, Lenhard et al. 2014, May, Knowlton et al. 2016). During exercise, the current study found significant differences in pregnant and non-pregnant women for the effects of the type of exercise (continuous vs. discontinuous) on HRV measures associate with sympathetic and parasympathetic modulation. A significant interaction of maternal condition and protocol type was observed during exercise.
for RMSSD, which was found to be higher by 38.1% in non-pregnant women during continuous exercise compared to pregnant women. Yet during discontinuous exercise, RMSSD was higher by 25.2% in pregnant women than non-pregnant women. As a time domain measure of beat-to-beat variance during exercise, RMSSD is used to estimate vagal-mediated changes in HRV, and is correlated with the high frequency (HF) power spectral component associated with parasympathetic modulation, and related to respiration activity (Electrophysiology 1996, Shaffer, McCraty et al. 2014).

No significant changes were observed in HF power measures relative to pregnancy and protocol, but there was a significant interaction observed for low frequency (LF) power. LF power was significantly higher in non-pregnant women compared to pregnant women during continuous exercise, but for discontinuous exercise, it was higher in pregnant women compared to non-pregnant women. The interpretation of LF power is controversial in the literature, in terms of whether it is a marker of both sympathetic modulation and vagal activity or sympathetic modulation only; and in relation to how measurement conditions (such as resting vs. ambulatory; normal breathing vs. paced breathing) impact this interpretation (Shaffer, McCraty et al. 2014).

The results of the current study show that RMSSD differences between pregnant and non-pregnant women suggesting higher vagal activity in non-pregnant women compared to pregnant women during continuous exercise, yet higher vagal activity for pregnant women during discontinuous exercise (compared to non-pregnant). In contrast, the higher LF observed for non-pregnant women during continuous exercise may indicate relatively higher sympathetic modulation than for pregnant women doing the same exercise. However, the opposite was observed for discontinuous exercise, with a higher LF in pregnant women compared to non-pregnant women. It is challenging to confirm exact differences between protocols based on pregnancy, due to the uncertainty of what LF power measures truly represents in this study. Furthermore, there is a scarcity of literature on gestational HRV responses during exercise to be able to draw on for comparison or clarity. Just one study was found to report on autonomic changes in pregnant women under acute exercising conditions (Avery, Wolfe et al. 2001), which
found that the increased sympathetic modulation during exercise was similar for pregnant and non-pregnant women, but that pregnant women had relatively less reduction of parasympathetic output. This was attributed to their already lowered parasympathetic modulation at rest. Therefore, the differences observed between groups during exercise in the present study may reflect the underlying differences in resting HRV between pregnant and non-pregnant women.

In healthy populations, relative changes in sympathetic and parasympathetic modulation and overall spectral power during exercise are influenced by the exercise intensity, with higher intensities associated with greater reduction in individual spectral power measures and total power, driven by relative sympathetic domination over vagal parasympathetic output (Robinson, Epstein et al. 1966, Perini and Veicsteinas 2003, White and Raven 2014). When the data of non-pregnant and pregnant participants were pooled for more robust comparisons between the two protocols performed at different exercise intensities, this revealed significant effects for some of the frequency domain measures. Continuous exercise was associated with higher LF for peak and relative measures of power, as well as higher relative HF power; while discontinuous exercise resulted in higher absolute LF power and greater LF/HF ratio. The interpretation of LF measures alone are not agreed on in the current literature, and LF/HF ratio is also one that can be misinterpreted in isolation, particularly from short-term recordings such as those used in this study (Electrophysiology 1996, Shaffer, McCraty et al. 2014). However, it has been suggested that under conditions where increased effort and greater sympathetic nervous system activation are present, such as during exercise, that a high LF/HF ratio (when also considered with individual HF and LF power) is indicative of greater sympathetic activity, relative to parasympathetic activity, (Shaffer, McCraty et al. 2014). It is interesting then to consider the findings of the current study discussed earlier where RMSSD, as a marker for vagal drive and associated with HF (parasympathetic modulation), was relatively higher in pregnant women (compared to non-pregnant women) during the moderate intensity, discontinuous exercise. This response could reflect the higher sympathetic input associated with the pregnant condition at baseline resting conditions.
Lastly, the current study observed that overall heart rate variability, as represented by the time-domain measure of SDNN, was significantly higher during discontinuous exercise compared to continuous exercise. Thus, the differences between the two protocols in the current study suggest discontinuous exercise had a relatively higher degree of sympathetic modulation (compared to parasympathetic) modulation. This may be reflective of the relatively higher exercise intensity (moderate vs. light) performed during this protocol. Higher exercise intensities are associated with a greater reduction in total power, as well as individual spectral power (Perini, Orizio et al. 1990, White and Raven 2014). In the current study, the relatively higher intensity of the exercise intervals during discontinuous protocol (compared to the continuous protocol) may have been offset by the interval structure that also included intervals of total rest. Therefore, the greater reduction in total power observed than what would be expected with moderate intensity compared to low intensity exercise may have been less than if the moderate intensity exercise was performed in a continuous structure.

The overall HRV findings of the current study give some preliminary new insights into acute exercise HRV responses in pregnant women, which may warrant further investigation of potential differences in sympathetic and parasympathetic modulation during discontinuous, or interval, structured exercise compared with continuous exercise, and responses observed in pregnant and non-pregnant women. However, there is also likely to be an impact of underlying baseline sympathetic modulation of pregnancy on the observed differences in exercising HRV responses between pregnant and non-pregnant groups. Additionally, the direct comparison of the two protocols with the participants' pooled show that a higher level of sympathetic modulation found during discontinuous exercise may be related to the higher intensity performed, rather than the difference in structure/continuity of exercise workload.
5.1.4 Acute exercise recovery

5.1.4.1 Post-prandial blood glucose

Exercise energy expenditure, rather than intensity, has been reported as the key variable for affecting glycaemic changes post-exercise (Larsen, Dela et al. 1997, Larsen, Dela et al. 1999). In the present study, post-prandial blood glucose response to a standardised snack was compared between a control condition (no exercise) on Day 1 and a post-exercise condition on Day 2, where a snack was consumed 15-minutes after exercise. No interaction was observed between the protocols over time for 1-hour post-prandial responses, in either pregnant or non-pregnant women. A previous study by Mottola, Wies et al. (1998) also reported no differences in post-prandial response in pregnant women compared to baseline, when given a high glucose load (75g oral glucose tolerance test) after 20 minutes of mild (30% VO\textsubscript{2peak}) cycling. Although the serve of carbohydrate provided in the current study was much less (13g); the exercise bouts undertaken were not dissimilar, considering the protocols of the current study: 30 minutes of continuous cycling performed at a workload for 25% VO\textsubscript{2peak} predicted, and the discontinuous protocol being matched for total work.

Based on the normal blood glucose levels across both groups, when participant groups were pooled to compare the two exercise protocols directly, without the primary variable of pregnancy, there was a significant blunting of 1-hour post-prandial BGL on Day 2 compared to Day 1, for each protocol. Following continuous and discontinuous exercise respectively, 1-hour post-prandial BGL was lowered by 16.9% (from 6.650 mmol.L\textsuperscript{-1} on Day 1 to 5.521 mmol.L\textsuperscript{-1} on Day 2) and 10.7% (from 6.557 mmol.L\textsuperscript{-1} on Day 1 to 5.850 mmol.L\textsuperscript{-1} on Day 2). A recent review on the influence of the timing and intensity of exercise on post-prandial levels concluded that aerobic exercise performed after a meal was more effective than exercise before a meal in both healthy and diabetic adults (Haxhi, Scotto di Palumbo et al. 2013). The exercise in the current study was performed pre-prandial, thus it was interesting to find both protocols were effective at significantly blunting post-prandial blood glucose. This suggests that undertaking exercise prior to a meal may have the potential to also be an effective strategy in blunting post-prandial BGL, however further research is needed in this area for any conclusive or specific recommendations.
5.1.4.2 Recovery metabolic responses

In the current study, no interaction was observed between pregnancy condition and exercise protocol on measures of recovery oxygen consumption (also known as post-exercise oxygen consumption, EPOC), respiratory exchange ratio or minute ventilation. Furthermore, no significant differences in the effects of each protocol were found when participants were pooled. However, when compared with baseline resting measures, both oxygen consumption and minute ventilation remained significantly elevated during the recovery period of the continuous, low intensity protocol but not the discontinuous, moderate intensity protocol. This contradicts previous literature that found exercise intensity to be the major determinant for EPOC, with higher intensities producing larger EPOC levels (Gore and Withers 1990, Larsen, Welde et al. 2014), but supports a more recent high intensity interval study that found no difference in EPOC levels relative to exercise intensity (Metcalfe, Koumanov et al. 2015).

Different exercise intensities in the current study did not produce differences in recovery respiratory exchange ratio, and comparison against baseline levels showed that both intensities led to significantly higher recovery oxygen consumption and suggesting that each protocol resulted in continued higher carbohydrate metabolism in short-term recovery. This is similar to an earlier study, where a bout of moderate intensity, continuous cycling did not produce different EPOC levels to a bout of high-intensity interval cycling with matched total work and duration (McGarvey, Jones et al. 2005).

5.1.4.3 Recovery HRV responses

There was no difference found in the HRV measures during exercise recovery, either related to interactions of pregnancy condition and protocol type, or between protocols. Earlier literature has shown that following low intensity exercise, autonomic control of HRV returns to baseline conditions within 5 minutes, with a dose-response of longer HRV changes related to higher exercise intensities (Perini, Orizio et al. 1990, Terziotti, Schena et al. 2001). Mourat, Bouhaddi et al (2004) compared effects of a single bout of each of continuous and interval exercise on HRV, and found during the first hour following interval exercise, there were greater decreases in total power and HF values, suggestive of a slower return of baseline parasympathetic (vagal) activity.
than after continuous exercise (Mourot, Bouhaddi et al. 2004). The investigation of recovery HRV differences between protocols in the current study may have also been limited by the chosen timing of the five-minute segment used for analysis. This was captured between minutes 2-7 of the 10-minute recovery phase. In contrast, a study that also used short-segment HRV for comparing exercise recovery following acute exercise of low, moderate and high intensities reported significant differences were mainly observed within the first minute (Michael, Jay et al. 2016). Therefore, the chosen time to capture recovery HRV measures in the current study is a likely limitation of being able to observe differences for HRV responses post-exercise, particularly given the lower exercise intensities used. Nevertheless, this adds a starting place to the literature in this field for future research, as no study has reported on recovery HRV measures in pregnant women following an acute bout of exercise.

5.2 Glycaemic control over 24 hours

5.2.1 Daily blood glucose variability

No significant interaction was observed between maternal condition and time for exercise effect on 24-hour mean blood glucose level and variability, for either continuous or discontinuous exercise. A recent meta-analysis of studies that used continuous glucose monitoring in type 2 diabetes concluded that acute exercise significantly decreased average daily blood glucose concentrations and time spent in hyperglycaemia range, with no effect on fasting or time in hypoglycaemia (MacLeod, Terada et al. 2013). Two of the studies included had also investigated glucose variability. One found no effect (Praet, Manders et al. 2006), while the other observed that variability was reduced following a single bout of moderate intensity exercise (Van Dijk, Manders et al. 2013). In contrast to a large volume of studies in type 2 diabetes; there have been no previous investigations either in general pregnancy or GDM women using continuous glucose monitoring to determine acute exercise effects on 24-hour glycaemic control. Although results of the current study provide a novel contribution to this area, the observations were found in women with a relatively normal baseline of glycaemic control (including those with GDM), based on the clinical glycaemic target values for gestational diabetes and type 2 diabetes (Inzucchi, Bergenstal et al. 2012, Nankervis, McIntyre et al. 2013). Thus, it would be important to repeat a similar investigation in GDM women who have greater dysfunction in glycaemic control (overall,
or for specific post-prandial responses) to determine whether exercise effects on 24-hour blood glucose control are different when baseline glycaemia is not optimal during pregnancy.

When the data from both groups were pooled in the current study to directly compare the exercise protocols, there were significant changes in 24-hour blood glucose levels and variability for the two exercise protocols. The mean 24-hour blood glucose level was significantly higher (5.64 mmol.L\(^{-1}\)) the day after discontinuous, moderate intensity exercise was undertaken, compared with the baseline day of no exercise (5.39 mmol.L\(^{-1}\)). This was unexpected given the opposite effects previously reported in type 2 diabetes, which found a single bout of exercise lowered 24-hour blood glucose levels (Van Dijk, Manders et al. 2013). Interestingly, a bout of low-intensity cycling significantly reduced 24-hour blood glucose level, whereas the higher intensity bout of cycling of equivalent total work had no effect (Manders, Van Dijk et al. 2010). In the current study, mean 24-hour blood glucose increased after discontinuous exercise, whereas continuous, low intensity protocol did not have any effect. It could be hypothesised that the difference in the direction of effect may be related to the difference in the baseline levels of glycaemic control between the type 2 diabetes cohort, and the women in the current study, where both pregnant and non-pregnant women had blood glucose levels within the normal range for optimal glycaemic control.

The standard deviation of all 24-hour blood glucose level was significantly lower following both continuous (16.5%) and discontinuous (19%) exercise, compared to Day 1 baseline. However, the 24-hour blood glucose level coefficient of variation was only reduced following discontinuous exercise. Additionally, discontinuous exercise was associated with higher mean blood glucose level overnight, and again with reduced variability, whereas there were no changes in overnight mean blood glucose level or variation following continuous exercise. Interestingly, both continuous and discontinuous exercise was observed to elicit higher recorded overnight minimum glucose levels, when compared to the minimum blood glucose level during the baseline night preceding each bout of exercise. Our findings contradict those of Bacchi, Negri et al. (2012) who reported that nocturnal glucose levels in individuals with type 2 diabetes were significantly lower following aerobic exercise compared with the previous day of no exercise.
Again, this discrepancy may in part be explained by the difference in baseline glycaemic measures between the type 2 diabetes study and the current study. Regardless, looking more broadly at the results of the current investigation, exercise intensity may be an important factor for reducing the variability of blood glucose concentrations following an acute exercise bout, when the findings of a reduction in 24-hour blood glucose variability following discontinuous, moderate intensity exercise but no difference in variability following continuous, low intensity exercise are considered together.

5.2.2 Post-prandial blood glucose response
Post-prandial hyperglycaemia is a clinical risk factor for cardiovascular complications (Stratton, Adler et al. 2000). In pregnancy, lower post-prandial blood glucose levels have been associated with fewer perinatal complications (Jacqueminet and Jannot-Lamotte 2010). In the current study, a single bout of continuous or discontinuous exercise both significantly blunted post-prandial blood glucose responses to a snack consumed shortly after exercise. However, there was no prolonged exercise effect on post-prandial BGL for a main meal consumed between 10 – 16 hours after exercise for either pregnant or non-pregnant women. The women in the current study had post-prandial blood glucose responses that fell within the clinical range for optimal glycaemic control in type 2 diabetes, as well as the lower target range for pregnancy [1-hr post-prandial ≤7.4mmol.L⁻¹; 2hr ≤6.7 mmol.L⁻¹] (Inzucchi, Bergenstal et al. 2012, Sullivan, Uman et al. 2012, Nankervis, McIntyre et al. 2013). Having groups with normal post-prandial responses may have limited the potential effect for any exercise-related prolonged changes.

In a study of women with GDM who had dysfunctional glycaemic control, a 30-minute bout of moderate intensity (60%VO₂max) cycling did not have any observed effect on next-day breakfast post-prandial response (Lesser, Gruppuso et al. 1996). In contrast, a type 2 diabetes study showed prolonged exercise effects in the 24 hours following exercise, with significant lowering of post-prandial blood glucose reduction following a 60-minute bout of moderate intensity (60% HRR) cycling (Oberlin, Mikus et al. 2014). The contrast in the responses observed between these two studies may be related to the pregnancy condition, the overall duration of the exercise (which was doubled in the latter study), or a combination. Looking at the effects of exercise structure,
Little, Jung et al. (2014) found that a single bout of high-intensity interval exercise, compared to moderate intensity continuous training of matched work, had a greater effect on improving post-prandial glycaemia over the following 24-hours (Little, Jung et al. 2014). This contrasts with Larsen, Dela et al. (1999) who found that it was the total energy expenditure, and not intensity, that was the key variable for exercise effect on post-prandial glucose responses in type 2 diabetes (Larsen, Dela et al. 1999). In the current study, the energy requirements of the exercise protocols, as a factor of the relative intensities and the durations, would be considerably less than the requirements for the exercise utilised undertaken in the study by Little, Jung et al (2014). This may have been a limiting factor preventing observation of any post-prandial responses beyond the acute exercise period, in either pregnant or non-pregnant women.

5.2.3 Fasting blood glucose

As was found for the post-prandial BGL responses, a single bout of continuous or discontinuous exercise had no significant effect on the fasting blood glucose measures captured the morning after exercise, compared to baseline fasting blood glucose levels. Pregnant condition also had no interaction with changes in fasting blood glucose levels between baseline and post-exercise. Early studies in GDM women failed to demonstrate any change in fasting blood glucose following a single bout of light or moderate intensity exercise (Lesser, Gruppuso et al. 1996, Avery and Walker 2001). Similarly, a short-term exercise study found that seven consecutive days of aerobic exercise training had no effect on fasting blood glucose levels in overweight or obese, sedentary adults with type 2 diabetes under free-living conditions (Mikus, Oberlin et al. 2012). Furthermore, after the completion of a 20-week exercise training program in healthy but sedentary participants, a single bout of exercise was found to increase fasting glucose levels, as well as decrease fasting insulin levels in the 24-hours following exercise (Boulé, Weisnagel et al. 2005). Thus, the potential for acute exercise to have a significant effect on fasting blood glucose levels in healthy or metabolic dysfunction populations has not yet been well established (MacLeod, Terada et al. 2013). Therefore, for pregnant women who may have difficulty with their fasting blood glucose levels but otherwise maintain good glycaemic control, a bout of exercise may not be an effective strategy for improving fasting levels in pregnancy.
In Australia, the fasting blood glucose level during pregnancy for diagnosis of GDM is ≥5.1 mmol.L⁻¹. Fasting for diagnostic purposes is done through a set protocol and measured from venous blood obtained through a medically-referred blood test. However, women are also required to self-monitor their fasting blood glucose levels, which is done using a glucometer and captures capillary blood glucose. For self-monitoring, fasting blood glucose is required to be ≤5.0 mmol.L⁻¹ as an indicator of good glycaemic control (Coustan, Lowe et al. 2010, Nankervis, McIntyre et al. 2013). Changes in GDM treatment, such as an indication to commence or increase insulin therapy, are often based on the self-measured blood glucose records, therefore there is some validity in comparing fasting levels from this study to those used to evaluate fasting levels in GDM. The current study found no carry-over effects from the acute exercise effect on fasting blood glucose levels for either group. Interestingly, the current study found that the mean fasting BGL in non-pregnant women after continuous exercise (4.84 mmol.L⁻¹) was the only measure that would meet the clinical threshold criteria (<5.1 mmol.L⁻¹) for appropriate fasting blood glucose control in pregnancy. Furthermore, the mean Day 1 fasting blood glucose levels, as measured by CGM, in non-pregnant participants (5.19 mmol.L⁻¹ in Phase 2, and 5.39 mmol.L⁻¹ in Phase 3) were also above the optimal glycaemic control threshold criteria used in pregnancy.

It is not clear whether the observed changes in overnight blood glucose in the current study had any direct interaction with fasting blood glucose levels the following morning. Following each protocol, the minimum blood glucose level recorded overnight on Day 2 was higher than during the Day 1 overnight period. After discontinuous exercise specifically, mean blood glucose overnight was also significantly higher than on Day 1. This is an area that would benefit from further investigation using more precise measurement of fasting blood glucose in pregnant women, including those diagnosed with gestational diabetes. If there was an association between exercise performed during the day and increases in overnight blood glucose with an effect on fasting blood glucose the following morning, there would be important practical implications for women who exercise regularly during pregnancy, and the clinical threshold level for fasting levels in the diagnostic criteria for GDM in Australia.
5.3 Perception of exercise exertion and enjoyment

The perceived physical exertion during either of the protocols was not affected by pregnancy; however, when groups were pooled, the RPE scores for overall exertion and for specific effort of the legs were both significantly higher during the discontinuous protocol, despite an equivalent metabolic cost between each exercise bout. This finding mirrors that found with high-intensity interval exercise in obese adults, where Little, Jung et al. (2014) observed RPE to be higher during high intensity interval exercise, compared with continuous moderate intensity exercise (Little, Jung et al. 2014). In contrast, a study of obese women with and without type 2 diabetes found RPE to be higher for continuous exercise compared with intermittent exercise bouts (reasonably matched for total work and duration) (Coquart, Lemaire et al. 2008). In that study, RPE was significantly lower during intermittent higher intensity exercise, than during continuous exercise of lower intensity. The authors related this to the concept of perceptual preference, where the lowest RPE was associated with the exercise conditions that were perceptually preferred by participants (Robertson and Noble 1997). The qualitative findings of the current study appear to contradict this finding. Although RPE was higher for discontinuous exercise, the majority of participants (12/14) also enjoyed the experience of the discontinuous protocol over the continuous protocol, which may be a reflection on previous findings that individuals are more likely to select an exercise intensity that corresponds with an RPE level between 10 – 14, as this range (light-moderate intensity) has been associated with a positive affective, or mood, response (Ekkekakis 2009).

Furthermore, when participants in the current study were asked at the end of their trial to qualitatively compare the relative difficulty of the two protocols, the responses were quite mixed. Just over half (8/14 participants) reported finding the discontinuous protocol either mildly (4) or moderately (4) more difficult, while more than a third felt there wasn’t a difference between the two (4/14). The remaining two participants found the continuous protocol moderately more difficult. These were both from the pregnancy group and identified that their breathing and overall fatigue levels were more noticeable during the continuous work without rest. Therefore, despite significantly higher reported levels of perceived exertion during the discontinuous exercise, the perception of comparative difficulty between the protocols was more mixed.
suggesting a variety of inputs are evaluated by individuals when it comes to exercise preferences (Duncombe, Wertheim et al. 2009, Evenson and Bradley 2010). From a clinical perspective, this has encouraging implications for exercise compliance. As observed in this study, a bout of discontinuous, moderate intensity exercise had significant and positive effects on acute blood glucose and 24-hour glycaemic variability and was perceived as requiring greater effort, and yet was perceived to be more enjoyable by pregnant and non-pregnant women with widely varying levels of fitness, physical activity and weight.

5.4 Resting measures

5.4.1 Baseline glycaemic control
Pregnant and non-pregnant women did not have significantly different baseline 24-hour blood glucose control. Furthermore, both groups in the study had relatively normal glycaemic levels compared with reference values for optimal glycaemic control, except that mean and peak fasting measures for the pregnant group (normoglycaemic and GDM women combined) were higher than the clinical threshold for GDM (Coustan, Lowe et al. 2010, Hernandez, Friedman et al. 2011, Nankervis, McIntyre et al. 2013). While the similarity of blood glucose measures between groups at baseline allowed for appropriate comparison of exercise effects on measures of glycaemic control, the actual effect of the exercise may have been less than what would be observed in women with less optimal glycaemic control. It also limits the extrapolation of results here to women with gestational diabetes or overt diabetes in pregnancy.

5.4.2 Baseline metabolic measures
Resting metabolic measures prior to exercise showed no differences in baseline oxygen consumption, respiratory exchange ratio or minute ventilation related to the interaction of pregnancy condition and protocol type. Similarly, when the two groups of participants were pooled, no difference was found in resting metabolic measures between the two protocols, therefore importantly demonstrating a similar baseline metabolic rate between the conditions of the study.
5.4.3 Resting heart rate variability

In pregnancy, there is a greater bias toward sympathetic modulation in response to demonstrated cardiovascular and metabolic adaptions associated with a normal pregnancy (Ekholm, Hartiala et al. 1997, Avery, Wolfe et al. 2001). The significantly lower pNN50 and RMSSD measures in the pregnant women at baseline for the current study align with relatively lower parasympathetic control. In addition, higher resting heart rate and shorter time between QRS intervals of beats (mean R-R interval) were observed in the pregnant women, further indicating higher resting sympathetic input. As an index of overall HRV, resting SDNN might also have been expected to be reduced in pregnant women. This comparison almost reached significance in the current study ($P=0.0573$), with a trend for lower SDDN in pregnant (32.80ms) compared to non-pregnant (64.91ms) women. Thus, the differences in resting HRV measures observed in the current study between pregnant and non-pregnant women reflect the well-established autonomic changes with pregnancy.

5.5 Study Limitations

Initially, the aim of this study was to compare three groups of women: i) pregnant with normoglycaemic control, ii) pregnant with diagnosed gestational diabetes (GDM), and iii) non-pregnant, with no known glycaemic dysfunction. Difficulties in recruiting women for both the healthy pregnancy and GDM groups led to participants in these two groups eventually being combined. This decision was made as it had been identified that the blood glucose levels for the GDM women who had participated in the study were within normal ranges (other than their diagnosed fasting BGL) throughout the study period. With the primary focus of the study being blood glucose responses to exercise, neither the glycaemic target ranges nor the exercise recommendations differ for GDM pregnancy compared to general pregnancy, thus this was not considered to be a limiting factor to changing the study groups. However, it did mean that some of the original design factors and the power calculation of the sample size and primary variable were no longer valid or ideal, and this has led to some challenges in justifying some areas within the current context of the study.
It is also recognised that the small sample size in combination with the normal propensity for large individual variation in blood glucose levels limits the strength and the applicability of the findings of the current study, particularly with respect to observing differences in glycaemic responses between pregnant and non-pregnant women. Furthermore, the fact that baseline glycaemic measures were normal in both groups may also have blunted or changed the exercise effects observed, in terms of the degree and/or direction of change.

The use of continuous glucose monitoring data, while novel for application of investigating exercise effects on glycaemic control in pregnancy, is not as accurate as direct measures of dysfunctional glycaemic control in pregnancy, such as blood tests for fasting levels in pregnancy. This study also did not measure insulin resistance, which would have added greater insight into underlying abnormal glycaemic control. As a pilot study, measuring insulin resistance was considered too invasive and not necessary for the current design. It is also a measure more likely to be affected by chronic exercise training, rather than a single bout of acute exercise. Additionally, the normal blood glucose levels across all the participants was not part of the study design, but an undesired outcome that was only identified after the analysis of the raw CGM data of several GDM participants. With this finding, having a measure of insulin resistance would have been an appropriate comparison to look at what was occurring with underlying physiological responses. However, as this characteristic was an undesired outcome, it wasn’t considered when making decisions about other study measures. Overall, the methods applied in this study were selected to capture glucose measures as practically and meaningfully as possible in a non-invasive way; however, it is recognised that they are not equivalent to the clinical testing procedures performed during pregnancy for screening and diagnosis of gestational diabetes.

Design-wise, this trial did not utilise a randomised or counter-balanced approach for the order of the exercise trials between participants. While there were practical reasons for this decision, the non-randomised study design may have also impacted the results, particularly with regards to the impact of food intake and self-measured BGL calibrations during each phase, as participants may have gotten better at maintaining their standardised diet, taking their BGLs and completing their study diary second time around, being the discontinuous protocol. Similarly, it may have
impacted ratings of perceived exertion and qualitative information on reported difficulty and enjoyment of each protocol.

The heterogeneity of the groups is another factor that may have influenced study outcomes, with regards to varying stages of gestation, body weight (pre-pregnancy), physical activity levels (pre and during pregnancy), health conditions that also affect hormone and metabolic processes (such as hypothyroid); and for the pregnancy group, the combination of normoglycaemic and GDM women into the same study group. For non-pregnant women, other factors that may also influence blood glucose responses, fatigue and metabolic measures such as prior pregnancy or phase of menstruation cycle, were not captured or controlled within the current design. However, an important focus of the pilot study was to investigate the effect of the exercise bouts under relatively free-living conditions, rather than being strictly controlled and all other variables standardised equally across all participants. One specific challenge in this design was matching daily physical activity levels of occupational work. While this was controlled within an individual’s trial to match work demands of Day 1 and Day 2, and in both phases wherever possible, this was not always achieved.

5.6 General Conclusions

This study was conducted to investigate the effects of a single bout of discontinuous, moderate intensity exercise on daily glycaemic control and acute blood glucose and cardiometabolic responses, as a novel stimulus in pregnant women. The study was designed to compare these responses to those following a bout of continuous, low intensity exercise of matched total work. Additionally, the study measured responses to both exercise bouts in a group of non-pregnant participants as a control. In pregnant women, a bout of discontinuous, moderate intensity cycling had a different interaction for acute blood glucose changes in compared to continuous exercise, yet both were positive and had significant reductions in blood glucose post-exercise. However, the same responses were not found in the non-pregnant women, suggesting there may be a difference in acute blood glucose responses following exercise in pregnant women, compared to non-pregnant women. For pregnant women, discontinuous exercise offers a practical and potentially effective option for short-term blood glucose reductions and was reported to be more enjoyable for most women, compared to traditional continuous exercise.
Daily glycaemic control was not affected by either type of exercise for either pregnant or non-pregnant women. When looking at the participants as a single group with normal blood glucose levels, discontinuous exercise did have an overall significant effect on improving measures of daily glucose variability, which was not observed for continuous exercise. This supports that exercise intensity is an important factor for improving measures of daily glycaemic variability, rather than only energy expenditure or overall duration of exercise. Differences observed in measures of sympathetic and parasympathetic modulation between pregnant and non-pregnant women relative to the type of exercise also reflect that either the exercise intensity, the intermittent structure of the exercise (with intervals of rest), or a combination of the two have a significant influence on relative sympathetic and parasympathetic balance during exercise in pregnant women. Metabolic work, substrate utilisation and respiratory effort were not affected by pregnancy condition during exercise or recovery for either type of exercise. However, discontinuous exercise (when pooled) did demonstrate a shift towards higher carbohydrate utilisation, which may be a contributing factor to the difference observed in daily glycaemic variability following discontinuous, but not continuous exercise.

Based on the findings of this study, the first hypothesis, being ‘A bout of discontinuous, moderate intensity cycling will elicit comparable acute glycaemic effects to a bout of continuous, low intensity cycling of matched total work in pregnant women; with similar responses observed in the non-pregnant control group’, is rejected. While there were similar acute blood glucose reductions following both exercise protocols in pregnant women, there was a different interaction found between the acute responses in pregnant compared to non-pregnant women, where the responses were not the same.

For the second hypothesis, ‘a bout of discontinuous, moderate intensity cycling will elicit different cardiometabolic responses during exercise and in the immediate post-exercise recovery period in pregnant women, compared with continuous, low intensity exercise’, this would be accepted, as there were significant differences observed in time (RMSSD) and frequency (Low Frequency – absolute power) responses to the exercise protocols in pregnant women, and also
when compared to non-pregnant women. However, these were the only significant responses identified, with no other changes observed in the remaining HRV measures, or with exercising oxygen consumption, respiratory exchange ratio or minute ventilation.

For the third hypothesis, ‘In pregnant women, a bout of discontinuous, moderate intensity cycling will reduce 24-hour blood glucose levels and variability after exercise compared with 24-hours preceding exercise. Comparatively, there will be no effect observed in pregnant women following a bout of continuous, low intensity exercise; or in non-pregnant controls following either discontinuous or continuous protocols’, this is rejected. There were no significant changes found in any 24-hour blood glucose measures following either protocol in pregnant or non-pregnant women.

Lastly, the fourth hypothesis, ‘In participants with normal daily glycaemic levels, a bout of discontinuous moderate intensity cycling will elicit comparable acute and 24-hour blood glucose responses, compared to a bout of continuous, low intensity exercise of equal total work, but double the volume of exercise’ is rejected. From the pooled data analysis, there were significant differences observed in the effect on 24-hour mean blood glucose and glucose variability following the discontinuous protocol, compared with the discontinuous protocol.

This novel pilot study has investigated the application of utilising interval exercise (described as discontinuous exercise in this thesis) at a moderate intensity to augment glycaemic control in pregnancy. It was found that 15 minutes of moderate intensity exercise, performed in a discontinuous nature, was effective at reducing acute blood glucose levels in both pregnant and non-pregnant women, meaning that interval exercise performed at moderate intensity may be an effective strategy for glycaemic effects. Further, it was well tolerated and enjoyed by participants without any adverse responses, suggesting that it may provide a comfortable and safe way for women to exercise at moderate intensities, in line with the pregnancy guidelines, without being limited by physical size, physical activity levels or current fitness.
The limitations of the study, in particular the small numbers and the design change from having women with gestational diabetes as a separate group, make the findings and applications of this work restricted. Future research in this area could replicate this original design of this study and include a GDM group to be able to truly evaluate the discontinuous exercise protocol for effect in managing 24-hour glycaemic control in women with overt hyperglycaemia. Future studies will also be able to confidently set the intensity protocols at less conservative levels, now that there are updated current pregnancy and exercise guidelines to support the safety and the effectiveness of moderate intensity exercise for all women with uncomplicated pregnancies. Lastly, it would be very interesting to gain a better understanding of the normal daily glycaemic profile in pregnant women, and in particular compare those who regularly exercise with those who are inactive to quantify how free-living physical activity patterns affect daily glycaemic control.

In conclusion, discontinuous, moderate intensity exercise totalling 15 minutes was equivalent to 30 minutes of continuous, low intensity exercise for beneficial effects on acute BGL response in pregnant participants. However, neither bout resulted in changes to daily blood glucose control. Further research is needed to identify discontinuous dose that augments daily glycaemic control in pregnancy.
CHAPTER SIX:

REFERENCES
6.1 REFERENCES


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CHAPTER SEVEN:

APPENDICES
PAR-Q+
The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

SECTION 1 - GENERAL HEALTH

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has your doctor ever said that you have a heart condition OR high blood pressure?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2. Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3. Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4. Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5. Are you currently taking prescribed medications for a chronic medical condition?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6. Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer NO if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7. Has your doctor ever said that you should only do medically supervised physical activity?</td>
<td>☐</td>
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</table>

If you answered NO to all of the questions above, you are cleared for physical activity.

Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow the Canadian Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
- If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or CSEP Certified Personal Trainer® (CSEP-CPT).
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:
- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant – talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes – please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.
<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>1. Do you have Arthritis, Osteoporosis, or Back Problems? If yes, answer questions 1a-1c if no, go to question 2</td>
<td></td>
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</tr>
<tr>
<td>2.1a</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
<td></td>
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</tr>
<tr>
<td>2.1b</td>
<td>Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylosis/pars defect (a crack in the bony ring on the back of the spinal column)?</td>
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<tr>
<td>2.1c</td>
<td>Have you had steroid injections or taken steroid tablets regularly for more than 3 months?</td>
<td></td>
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<tr>
<td>2.2</td>
<td>2. Do you have Cancer of any kind? If yes, answer questions 2a-2b if no, go to question 3</td>
<td></td>
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<tr>
<td>2.2a</td>
<td>Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and neck?</td>
<td></td>
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<tr>
<td>2.2b</td>
<td>Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?</td>
<td></td>
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</tr>
<tr>
<td>2.3</td>
<td>3. Do you have Heart Disease or Cardiovascular Disease? This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3a</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
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<tr>
<td>2.3b</td>
<td>Do you have an irregular heart beat that requires medical management? (e.g. atrial brillation, premature ventricular contraction)</td>
<td></td>
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<tr>
<td>2.3c</td>
<td>Do you have chronic heart failure?</td>
<td></td>
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<tr>
<td>2.3d</td>
<td>Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer YES if you do not know your resting blood pressure)</td>
<td></td>
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<tr>
<td>2.3e</td>
<td>Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?</td>
<td></td>
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<tr>
<td>2.4</td>
<td>4. Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes</td>
<td></td>
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<tr>
<td>2.4a</td>
<td>Is your blood sugar often above 13.0 mmol/L? (Answer YES if you are not sure)</td>
<td></td>
<td></td>
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<tr>
<td>2.4b</td>
<td>Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?</td>
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<td></td>
</tr>
<tr>
<td>2.4c</td>
<td>Do you have other metabolic conditions (such as thyroid disorders, pregnancy-related diabetes, chronic kidney disease, liver problems)?</td>
<td></td>
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<tr>
<td>2.5</td>
<td>5. Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome</td>
<td></td>
<td></td>
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<tr>
<td>2.5a</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5b</td>
<td>Do you also have back problems affecting nerves or muscles?</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Please read the questions below carefully and answer each one honestly: check YES or NO.</td>
<td>YES</td>
<td>NO</td>
</tr>
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<tr>
<td>6.</td>
<td>Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure</td>
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<td></td>
<td>If yes, answer questions 6a-6d  If no, go to question 7</td>
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<tr>
<td>6a.</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
<td></td>
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</tr>
<tr>
<td>6b.</td>
<td>Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?</td>
<td></td>
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<tr>
<td>6c.</td>
<td>If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?</td>
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<tr>
<td>6d.</td>
<td>Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?</td>
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<tr>
<td>7.</td>
<td>Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia</td>
<td>If yes, answer questions 7a-7c  If no, go to question 8</td>
<td></td>
</tr>
<tr>
<td>7a.</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
<td></td>
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<tr>
<td>7b.</td>
<td>Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?</td>
<td></td>
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<tr>
<td>7c.</td>
<td>Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?</td>
<td></td>
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<tr>
<td>8.</td>
<td>Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event</td>
<td>If yes, answer questions 8a-c  If no, go to question 9</td>
<td></td>
</tr>
<tr>
<td>8a.</td>
<td>Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)</td>
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</tr>
<tr>
<td>8b.</td>
<td>Do you have any impairment in walking or mobility?</td>
<td></td>
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<tr>
<td>8c.</td>
<td>Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?</td>
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<tr>
<td>9.</td>
<td>Do you have any other medical condition not listed above or do you live with two chronic conditions?</td>
<td>If yes, answer questions 9a-c  If no, read the advice on page 4</td>
<td></td>
</tr>
<tr>
<td>9a.</td>
<td>Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months OR have you had a diagnosed concussion within the last 12 months?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9b.</td>
<td>Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9c.</td>
<td>Do you currently live with two chronic conditions?</td>
<td></td>
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</table>

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.
PAR-Q+

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

› It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) to help you develop a safe and effective physical activity plan to meet your health needs.
› You are encouraged to start slowly and build up gradually – 20-60 min. of low- to moderate-intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
› As you progress, you should aim to accumulate 150 minutes or more of moderate-intensity physical activity per week.
› If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the follow-up questions about your medical condition:

› You should seek further information from a licensed health care professional before becoming more physically active or engaging in a fitness appraisal and/or visit a or qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

› You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
› You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
› Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

› You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
› The Canadian Society for Exercise Physiology, the PAR-Q+ Collaboration, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
› If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.
› Please read and sign the declaration below:

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME ____________________________________________________ DATE _________________________________________

SIGNATURE _____________________________________WITNESS _________________________________________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER __________________________________________________________

For more information, please contact:
Canadian Society for Exercise Physiology
www.csep.ca

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or BC Ministry of Health Services.

KEY REFERENCES
PARmed-X for PREGNANCY is a guideline for health screening prior to participation in a prenatal fitness class or other exercise.

Healthy women with uncomplicated pregnancies can integrate physical activity into their daily living and can participate without significant risks either to themselves or to their unborn child. Postulated benefits of such programs include improved aerobic and muscular fitness, promotion of appropriate weight gain, and facilitation of labour. Regular exercise may also help to prevent gestational glucose intolerance and pregnancy-induced hypertension.

The safety of prenatal exercise programs depends on an adequate level of maternal-fetal physiological reserve. PARmed-X for PREGNANCY is a convenient checklist and prescription for use by health care providers to evaluate pregnant patients who want to enter a prenatal fitness program and for ongoing medical surveillance of exercising pregnant patients.

Instructions for use of the 4-page PARmed-X for PREGNANCY are the following:

1. The patient should fill out the section on PATIENT INFORMATION and the PRE-EXERCISE HEALTH CHECKLIST (PART 1, 2, 3, and 4 on p. 1) and give the form to the health care provider monitoring her pregnancy.
2. The health care provider should check the information provided by the patient for accuracy and fill out SECTION C on CONTRAINDICATIONS (p. 2) based on current medical information.
3. If no exercise contraindications exist, the HEALTH EVALUATION FORM (p. 3) should be completed, signed by the health care provider, and given by the patient to her prenatal fitness professional.

In addition to prudent medical care, participation in appropriate types, intensities and amounts of exercise is recommended to increase the likelihood of a beneficial pregnancy outcome. PARmed-X for PREGNANCY provides recommendations for individualized exercise prescription (p. 3) and program safety (p. 4).

NOTE: Sections A and B should be completed by the patient before the appointment with the health care provider.
**Prescription for Aerobic Activity**

**RATE OF PROGRESSION:** The best time to progress is during the second trimester since risks and discomforts of pregnancy are lowest at that time. Aerobic exercise should be increased gradually during the second trimester from a minimum of 15 minutes per session, 3 times per week (at the appropriate target heart rate or RPE) to a maximum of approximately 30 minutes per session, 4 times per week (at the appropriate target heart rate or RPE).

**WARM-UP/COOL-DOWN:** Aerobic activity should be preceded by a brief (10-15 min.) warm-up and followed by a short (10-15 min.) cool-down. Low intensity calisthenics, stretching and relaxation exercises should be included in the warm-up/cool-down.

**PRESCRIPTION/MONITORING OF INTENSITY:** The best way to prescribe and monitor exercise is by combining the heart rate and rating of perceived exertion (RPE) methods.

**HEART RATE RANGES FOR PREGNANT WOMEN**

<table>
<thead>
<tr>
<th>MATERNAL AGE</th>
<th>FITNESS LEVEL or BMI</th>
<th>HEART RATE RANGE (beats/minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20</td>
<td>-</td>
<td>140-155</td>
</tr>
<tr>
<td>20-29</td>
<td>Low</td>
<td>129-144</td>
</tr>
<tr>
<td></td>
<td>Active</td>
<td>135-150</td>
</tr>
<tr>
<td></td>
<td>Fit</td>
<td>145-160</td>
</tr>
<tr>
<td></td>
<td>BMI&gt;25 kg m²</td>
<td>102-124</td>
</tr>
<tr>
<td>30-39</td>
<td>Low</td>
<td>128-144</td>
</tr>
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<td></td>
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<td>130-145</td>
</tr>
<tr>
<td></td>
<td>Fit</td>
<td>140-156</td>
</tr>
<tr>
<td></td>
<td>BMI&gt;25 kg m²</td>
<td>101-120</td>
</tr>
</tbody>
</table>

Target HR ranges were derived from peak exercise tests in medically prescreened low-risk women who were pregnant. (Mottola et al., 2006; Davenport et al., 2008).

**“TALK TEST”** - A final check to avoid overexertion is to use the “talk test”. The exercise intensity is excessive if you cannot carry on a verbal conversation while exercising.

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The original PARmed-X for PREGNANCY was developed by L.A. Wolfe, Ph.D., Queen’s University and updated by Dr. M.F. Mottola, Ph.D., University of Western Ontario.

No changes permitted. Translation and reproduction in its entirety is encouraged.

Disponible en français sous le titre «Examination medicale sur l’aptitude à l’activité physique pour les femmes enceintes (X-AAP pour les femmes enceintes)»

Additional copies of the PARmed-X for PREGNANCY, can be downloaded from Canadian Society for Exercise Physiology [www.csep.ca/forms](http://www.csep.ca/forms)
PARmed-X for PREGNANCY

PRESCRIPTION FOR MUSCULAR CONDITIONING DURING PREGNANCY

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>EFFECTS OF PREGNANCY</th>
<th>EXERCISE MODIFICATIONS</th>
</tr>
</thead>
</table>
| Body Position                 | • in the supine position (lying on the back), the enlarged uterus may either decrease the flow of blood returning from the lower half of the body as it presses on a major vein (inferior vena cava) or it may decrease flow to a major artery (abdominal aorta) | • past 4 months of gestation, exercises normally done in the supine position should be altered  
  • such exercises should be done side lying or standing |
| Joint Laxity                  | • ligaments become relaxed due to increasing hormone levels                          | • avoid rapid changes in direction and bouncing during exercises                         |
| Abdominal Muscles             | • presence of a rippling (bulging) of connective tissue along the midline of the pregnant abdomen (diastasis recti) may be seen during abdominal exercise | • abdominal exercises are not recommended if diastasis recti develops                    |
| Posture                       | • increasing weight of enlarged breasts and uterus may cause a forward shift in the centre of gravity and may increase the arch in the lower back  
  • this may also cause shoulders to slump forward | • emphasis on correct posture and neutral pelvic alignment. Neutral pelvic alignment is found by bending the knees, feet shoulder width apart, and aligning the pelvis between accentuated lordosis and the posterior pelvic tilt position. |
| Precautions for Resistance Exercise | • emphasis must be placed on continuous breathing throughout exercise  
  • exhale on exertion, inhale on relaxation using high repetitions and low weights  
  • Valsalva Manoeuvre (holding breath while working against a resistance) causes a change in blood pressure and therefore should be avoided  
  • avoid exercise in supine position past 4 months gestation | |

EXERCISE MODIFICATIONS

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  • exhale on exertion, inhale on relaxation using high repetitions and low weights  
  • Valsalva Manoeuvre (holding breath while working against a resistance) causes a change in blood pressure and therefore should be avoided  
  • avoid exercise in supine position past 4 months gestation  

PRECAUTIONS FOR MUSCULAR CONDITIONING DURING PREGNANCY

<table>
<thead>
<tr>
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<th>PURPOSE</th>
<th>EXAMPLE</th>
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<tr>
<td>Upper back</td>
<td>Promotion of good posture</td>
<td>Shoulder shrugs, shoulder blade pinch</td>
</tr>
<tr>
<td>Lower back</td>
<td>Promotion of good posture</td>
<td>Modified standing opposite leg &amp; arm lifts</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Promotion of good posture, prevent low-back pain, prevent diastasis recti, strengthen muscles of labour</td>
<td>Abdominal tightening, abdominal curl-ups, head raises lying on side or standing position</td>
</tr>
<tr>
<td>Pelvic floor</td>
<td>Promotion of good bladder control, prevention of urinary incontinence</td>
<td>“Wave”, “elevator”</td>
</tr>
<tr>
<td>Upper body</td>
<td>Improve muscular support for breasts</td>
<td>Shoulder rotations, modified push-ups against a wall</td>
</tr>
<tr>
<td>Buttocks, lower limbs</td>
<td>Facilitation of weight-bearing, prevention of varicose veins</td>
<td>Buttocks squeeze, standing leg lifts, heel raises</td>
</tr>
</tbody>
</table>

WARM-UPS & COOL DOWN:

Range of Motion: neck, shoulder girdle, back, arms, hips, knees, ankles, etc.

Static Stretching: all major muscle groups (DO NOT OVER STRETCH)

EXAMPLES OF MUSCULAR STRENGTHENING EXERCISES

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PARmed-X for Pregnancy - Health Evaluation Form

(to be completed and given to the prenatal fitness professional after obtaining medical clearance to exercise)

I, ________________________________, PLEASE PRINT (patient’s name), have discussed my plans to participate in physical activity during my current pregnancy with my health care provider and I have obtained his/her approval to begin participation.

Signed: ________________________________  
(patient’s signature)

Date: ________________________________

Name of health care provider: ________________________________

Address: ________________________________  
_________________________________________  
_________________________________________  
Telephone: ________________________________

HEALTH CARE PROVIDER’S COMMENTS:

_________________________________________  
_________________________________________  
_________________________________________  
_________________________________________  
(health care provider’s signature)
Advice for Active Living During Pregnancy

Pregnancy is a time when women can make beneficial changes in their health habits to protect and promote the healthy development of their unborn babies. These changes include adopting improved eating habits, abstinence from smoking and alcohol intake, and participating in regular moderate physical activity. Since all of these changes can be carried over into the postnatal period and beyond, pregnancy is a very good time to adopt healthy lifestyle habits that are permanent by integrating physical activity with enjoyable healthy eating and a positive self and body image.

**Active Living:**
- see your doctor before increasing your activity level during pregnancy
- exercise regularly but don’t overexert
- exercise with a pregnant friend or join a prenatal exercise program
- follow FITT principles modified for pregnant women
- know safety considerations for exercise in pregnancy

**Healthy Eating:**
- the need for calories is higher (about 300 more per day) than before pregnancy
- follow Canada’s Food Guide to Healthy Eating and choose healthy foods from the following groups: whole grain or enriched bread or cereal, fruits and vegetables, milk and milk products, meat, fish, poultry and alternatives
- drink 6-8 glasses of fluid, including water, each day
- salt intake should not be restricted
- limit caffeine intake i.e., coffee, tea, chocolate, and cola drinks
- dieting to lose weight is not recommended during pregnancy

**Positive Self and Body Image:**
- remember that it is normal to gain weight during pregnancy
- accept that your body shape will change during pregnancy
- enjoy your pregnancy as a unique and meaningful experience

For more detailed information and advice about pre- and postnatal exercise, you may wish to obtain a copy of a booklet entitled *Active Living During Pregnancy: Physical Activity Guidelines for Mother and Baby* © 1999. Available from the Canadian Society for Exercise Physiology, www.csep.ca. Cost: $11.95


