Cycling to break the cycle of diabetes in pregnancy: The role of exercise in the prevention of gestational diabetes mellitus

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**Executive overview**

Gestational diabetes mellitus (GDM) affects an increasing number of women worldwide, with the recurrence rate of this condition being as high as 69%. To date, few randomised controlled trials have examined the effects of regular antenatal exercise on the prevention of GDM and no previous studies have specifically sampled women with a history of GDM in a prior pregnancy, who are at high-risk of recurrence. Unfortunately, the barriers to exercise experienced by this population of women are often exacerbated, since they have existing children to care for, along with other household/work responsibilities and a lack of time. Given that low adherence rates to exercise has been highlighted as a limitation in some previous studies reporting regular exercise to be ineffective in preventing GDM, consideration must be given to the design of exercise interventions for the pregnant woman. Supervised, home-based exercise may effectively remove the issues of child care availability and transportation faced by pregnant women consequently enhancing opportunities for exercise engagement. However, the specific format and intensity of exercise to safely optimise benefits for health and fitness for pregnant women is not known.

The first study of this thesis (Chapter 2) examined how the addition of brief, self-paced, higher intensity intervals to traditional continuous moderate intensity exercise affected energy expenditure and the enjoyment of exercise in pregnant women. This was important to determine given that any additional energy expenditure resulting from higher intensity intervals may be meaningless if enjoyment is compromised, since long-term adherence would likely be low. Twelve healthy pregnant women in their third trimester (30 ± 1 weeks gestation; age 35 ± 6 y; BMI 27.1 ± 4.3 kg/m$^2$) performed either (i) continuous stationary cycling (CONT) at a steady power output equivalent to 65%
age-predicted heart rate maximum or (ii) interval cycling (INTV) consisting of continuous cycling at the same power output as CONT, but with the addition of six 15-s self-paced higher intensity efforts performed at regular intervals. Mean cycling power output, heart rate, oxygen consumption and energy expenditure were higher during INTV compared with CONT ($P < 0.05$), suggesting that the addition of as little as six 15-s intervals (90 s in total) to a 30 min bout of continuous moderate intensity exercise effectively increases overall energy expenditure. Despite this overall higher intensity, there was no difference in the mean rate of perceived exertion between conditions, while the enjoyment of exercise was higher with INTV ($P = 0.01$).

Given that interval-type cycling was found to effectively increase energy expenditure and enhance the enjoyment of exercise compared with traditional continuous cycling in pregnant women, the second study of this thesis (Chapter 3) was a randomised controlled trial that investigated the effects of a 14-week supervised, home-based exercise program of interval stationary cycling on the recurrence of GDM in women with a history of this condition in a previous pregnancy. The secondary aims of the study included examining the effects of the exercise intervention on maternal cardiovascular fitness, body anthropometrics, psychological well-being and obstetric outcomes. From June 2011 to July 2014, 172 women with a history of GDM (age 33.7 ± 4.0 y; BMI 26.1 ± 5.3 kg/m$^2$) were randomised into either an exercise intervention (EX; n = 85) or standard routine antenatal care (CON; n = 87) at 13 ± 1 weeks gestation. The intervention involved 14 weeks of supervised, home-based exercise on a stationary cycle ergometer, performed three times a week for 30 – 60 min. Overall compliance to the intervention was 83%. Based on an intention-to-treat analysis, the recurrence of GDM was similar between groups (EX, 40.5%; CON, 40.0%), and there was no
difference in the overall degree of glucose tolerance or insulin response to a 75 g oral glucose tolerance test between groups post-intervention (28 ± 1 weeks; $P > 0.05$). However, significant improvements in maternal cardiovascular fitness were observed in EX, resulting in higher fitness in EX compared with CON post-intervention ($P = 0.001$).

In addition, psychological distress (depression, anxiety and stress) assessed by the Depression Anxiety and Stress Scale$^{21}$ was significantly reduced in EX compared with CON post-intervention ($P < 0.05$). Importantly, there were no differences in obstetric and neonatal outcomes observed between groups suggesting that the exercise intervention had no adverse effects on fetal well-being during pregnancy.

Overall, the findings of this thesis suggest that a regular program of supervised, home-based exercise commenced from the first trimester of pregnancy does not prevent GDM in women with a history of the condition. However, the intervention was successful in overcoming barriers to exercise in pregnancy, promoting high adherence to the exercise program and providing important benefits for maternal cardiovascular fitness and psychological well-being. Despite the lack of effect of the intervention on GDM recurrence observed here, future studies are needed to determine whether the commencement of a regular program of exercise earlier in pregnancy, or even prior to conception affect the incidence of GDM.
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**List of abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>ANOVA</td>
<td>analysis of variance</td>
</tr>
<tr>
<td>AUC</td>
<td>area under curve</td>
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<tr>
<td>BMI</td>
<td>body mass index</td>
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<tr>
<td>bpm</td>
<td>beats per minute</td>
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<tr>
<td>CON</td>
<td>control group (Chapter 3)</td>
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<td>CONT</td>
<td>continuous exercise trial</td>
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<tr>
<td>DASS&lt;sub&gt;21&lt;/sub&gt;</td>
<td>Depression Anxiety Stress Scale</td>
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<tr>
<td>EPDS</td>
<td>Edinburgh postnatal depression scale</td>
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<tr>
<td>EX</td>
<td>exercise intervention group (Chapter 3)</td>
</tr>
<tr>
<td>FFA</td>
<td>free fatty acid</td>
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<tr>
<td>GCT</td>
<td>glucose challenge test</td>
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<tr>
<td>GDM</td>
<td>gestational diabetes mellitus</td>
</tr>
<tr>
<td>GLUT-4</td>
<td>glucose transporter protein 4</td>
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<tr>
<td>HbA1c</td>
<td>glycosylated haemoglobin</td>
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<tr>
<td>HDL</td>
<td>high density lipoprotein</td>
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<tr>
<td>hGH</td>
<td>human growth hormone</td>
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<tr>
<td>HOMA-IR</td>
<td>homeostasis model of assessment-insulin resistance</td>
</tr>
<tr>
<td>hPL</td>
<td>human placental lactogen</td>
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<tr>
<td>HR</td>
<td>heart rate</td>
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<tr>
<td>HR&lt;sub&gt;max&lt;/sub&gt;</td>
<td>heart rate maximum</td>
</tr>
<tr>
<td>INTV</td>
<td>interval exercise trial</td>
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<tr>
<td>IRSD</td>
<td>Index of Relative Socio-economic Advantage and Disadvantage</td>
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<tr>
<td>ISI</td>
<td>insulin sensitivity indices</td>
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<td>kJ</td>
<td>kilojoules</td>
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LDL  low density lipoprotein
MNT  medical nutritional therapy
OGTT oral glucose tolerance test
PACES Physical Activity Enjoyment Scale
RPE rate of perceived exertion
SEIFA socio-economic indexes for areas
SPAS Social Physique Anxiety Scale
TNF-α tumor necrosis factor alpha
W watts
\( \dot{V}O_2 \) rate of oxygen consumption
\( \dot{V}O_2\text{max} \) maximal aerobic capacity
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Statement of candidate contribution

The acute study (Chapter 2) was designed and conducted by M.J Ong under the guidance and assistance of Dr Kym Guelfi, Professor Paul Fournier, Dr Karen Wallman and Professor John Newnham (the candidate’s supervisors). All participant recruitment and management of the acute study was carried out by the PhD candidate, along with the organisation, implementation and performance of all experimental trials described.

The randomised controlled trial (The Cycle Study; Chapter 3) described in this thesis was designed by a team of investigators at The University of Western Australia, led by Professor John Newnham, and including Dr Kym Guelfi, Professor Paul Fournier, Dr Karen Wallman, Adjunct Professor Dorota Doherty and Professor Bob Grove. Recruitment of the study was managed by Research Midwives Cherry Young and Diana Loh of the Women and Infants Research Foundation. The day-to-day implementation of The Cycle Study was conducted under the supervision of the investigators by M.J. Ong (the PhD candidate) and Dr Nicole Crisp (Research Officer). The exercise intervention was delivered by M.J. Ong (the Candidate), Dr Nicole Crisp and a team of 14 casual exercise physiologists over the 3.5 years of data collection.

Part of the data analysis of The Cycle Study (Chapter 3) and all of the data analysis of the acute study (Chapter 2), along with original drafting of the thesis and manuscripts were the responsibility of the candidate. The candidate’s supervisors have provided
feedback for subsequent drafts and review of the thesis and manuscript, with assistance in the analysis of results by Adjunct Professor Dorota Doherty and Mr James Humphreys. Adjunct Professor Dorota Doherty and Professor Bob Grove also reviewed and provided feedback to sections of Chapter 3 pertaining to their expertise.

Permission has been given by Dr Kym Guelfi, Professor Paul Fournier, Dr Karen Wallman and Professor John Newnham for the manuscript (Chapter 2) listed on page 61 to be included in this thesis.
Chapter 1

Literature review
1.1 Introduction

Gestational diabetes mellitus (GDM) is a common medical complication of pregnancy. Although the hyperglycemia associated with GDM usually resolves itself naturally postpartum, there is increased risk of many acute and long-term health problems for the mother and her child, calling for a preventive strategy to reduce its manifestation and recurrence. While regular exercise during pregnancy offers numerous benefits, its role in preventing GDM remains inconclusive. This literature review will explain the pathophysiology, risk factors and implications of the condition and discuss current research on the effects of regular exercise during pregnancy on the incidence and severity of GDM. Current barriers to exercise participation in pregnancy and potential solutions will also be discussed.

1.2 Physiological adaptations to pregnancy

Following the fertilisation of an ovum by a sperm and successful implantation into the uterine wall, the secretion of pregnancy-related hormones triggers a series of physiological changes to prepare a woman’s body for the growth of the fetus and the increased metabolic demands of pregnancy. These changes influence a number of body systems with implications for cardiovascular, respiratory, endocrine and thermoregulatory control. For example, estrogen increases the blood volume by as much as 50% compared with normal blood volume by the end of pregnancy (Williamson, 2011). This leads to an increase in cardiac output by 30 - 50 % and an increase in resting maternal heart rate by 10 – 15 beats per minute (bpm) along with an increase in stroke volume (Artal, Wiswell & Drinkwater, 1991; Morton, 1991; Williamson, 2011). Likewise, there is a 50 % increase in minute ventilation, due to a large increase in tidal volume and a slight increased rate of respiration (Artal, Wiswell, Romem & Dorey,
Metabolically, maternal blood triglycerides, fatty acids and plasma cholesterol levels increase to support the increase in maternal energy demands (Williamson, 2011). At the same time, the pregnant woman experiences a natural progressive increase in insulin resistance to ensure adequate glucose for fetal development (Herrera, 2000). This change has important implications for the potential development of GDM as outlined below.

1.3 Insulin resistance during pregnancy

Insulin resistance can increase by up to 50% in a normal pregnancy compared with the pre-pregnancy state (Catalano, Huston, Amini, & Kalhan, 1999; Catalano et al., 1993). This increase in insulin resistance occurs gradually as pregnancy progresses, with the resistance to insulin in the first trimester remaining similar or decreasing slightly from pre-pregnancy states, but worsening as pregnancy advances into the third trimester to ensure that circulating blood glucose is readily available to the growing fetus when it is most needed (Herrera, 2000).

The cause of increased insulin resistance during pregnancy is multifactorial. First, insulin resistance is contributed to by the increasing concentration of many circulating hormones in the mother as the placenta develops, including progesterone, prolactin, cortisol, human placental lactogen and human placental growth hormone (Brelje et al., 1993; Handwerger & Freemark, 2000; Lain & Catalano, 2007). The diabetogenic action of these hormones has been illustrated through experiments involving the administration of exogenous human placental lactogen, progesterone or glucocorticoids to non-pregnant individuals (Kalkhoff, Jacobson, & Lemper, 1970; Kalkhoff, Richardson, & Beck, 1969; Samaan, Yen, Gonzalez, & Pearson, 1968). In these studies, non-pregnant
participants replicated glycaemic states of pregnancy, with elevated fasting blood glucose levels and increased insulin secretion to maintain normoglycemia (Kalkhoff et al., 1970; Kalkhoff et al., 1969; Samaan et al., 1968).

There is also evidence that the concentration of circulating free fatty acids (FFA) contribute to the increase in insulin resistance during pregnancy (Simmons, 2011; Sivan & Boden, 2003; Sivan et al., 1998). Between the 10th and the 30th week of pregnancy, maternal adipose stores increase markedly so that in the final trimester (where fetal growth is at its greatest), there is an energy reserve of approximately 30,000 kcal (123 600 kJ) from fat stores for the mother (King, 2003). This shift towards using fat stores as the main maternal energy source ensures that circulating glucose is primarily used for fetal development (Butte, 2000). Concurrently, the shift towards lipolysis for energy leads to increasing levels of plasma FFA, which leads to an increase in insulin resistance with advancing gestation (Sivan & Boden, 2003; Sivan et al., 1998).

Another contributing factor to increased insulin resistance in pregnancy is a reduction in circulating adiponectin concentrations. Adiponectin reduces insulin resistance through increased fatty acid oxidation and inhibition of hepatic glucose production (Lihn, Pedersen, & Richelsen, 2005). Accordingly, the reduction in adiponectin concentration in the blood as gestation progresses contributes to the increase in insulin resistance in pregnancy (Altinova et al., 2007; Barbour et al., 2007; Kinals, Telejko, Kuzmicki, Kretowski, & Kinalska, 2005). Likewise, impairments in glucose transport may be influenced by placenta-derived cytokines such as tumor necrosis factor alpha (TNF-α). This cytokine, TNF-α impairs insulin signaling via the pathway of insulin receptor substrate-1 autophosphorylation (Lain & Catalano, 2007). Of note, TNF-α concentration
is shown to directly correlate to changes in maternal insulin resistance, highlighting its impact on the condition (Kirwan et al., 2002). In combination, the aforementioned factors negatively affect the translocation of insulin-regulated glucose transporter type 4 (or GLUT-4) required for glucose uptake, causing a progressive worsening of insulin resistance as pregnancy advances.

1.4 Insulin secretion and glucose tolerance in normal pregnancy

The relationship between insulin secretion and insulin sensitivity presents itself in a negative feedback loop, whereby the pancreatic β-cells compensate for changes in whole-body insulin sensitivity through a proportionate and reciprocal change in insulin secretion (Bergman, Ader, Huecking, & Van Citters, 2002; Kahn, 2003). In response to this worsening of insulin resistance in a pregnant woman, there is a 200-250% compensatory rise in insulin secretion (Catalano et al., 1999) to maintain blood glucose levels within pre-prandial ranges of 5.3 - 5.5 mmol/L (Crowther et al., 2005). Interestingly, in the first trimester, there is an increased insulin response to glucose, regardless of the state of insulin resistance in the woman, although the mechanism for this has yet to be established (Catalano, 2014; Catalano et al., 1999; Catalano et al., 1993). However, by the third trimester of pregnancy, the stimulus for the β-cells to increase the rate of insulin secretion in the mother comes from a combination of both the pregnancy-related hormones and the increasing levels of insulin resistance (Lain & Catalano, 2007). Accordingly, responsiveness of the β-cells to pregnancy-induced insulin resistance is vital for normal glucose regulation during pregnancy.
1.5 The pathophysiology of gestational diabetes mellitus

Alas, if this compensatory relationship between insulin secretion and insulin sensitivity, first described by Kahn et al. (1993) fails, and insulin secretion is unable to overcome the degree of insulin resistance, impaired glucose tolerance ensues, resulting in chronic hyperglycemia in pregnancy, progressively worsening until delivery if not managed appropriately. This state of glucose intolerance with onset or first recognition during pregnancy is known as GDM (Metzger, 1991). The precise reason why the compensatory increase in insulin secretion fails in some pregnancies, leading to GDM is not clear, although research has shown that the factors contributing to insulin resistance in pregnancy may be exacerbated in women with GDM. Of note, FFA levels in pregnant women with GDM were reported to be significantly higher than pregnant women without GDM (Meyer, Calvert, & Moses, 1996). Similarly, plasma adiponectin concentrations have been observed to be significantly lower in women with GDM compared with women without GDM (Worda et al., 2004). Furthermore, serum TNF-α levels, while elevated in normal pregnancy, were found to be significantly higher in women with GDM when compared with pregnant women with normal glucose tolerance (Altinova et al., 2007; Kinalsiki et al., 2005). Women with GDM also appear to have reduced GLUT-4 activity, with a 65% decrease in insulin-stimulated glucose transport compared with women without GDM. Of note, this reduction is significantly worse than that observed in obese women with normal glucose tolerance (Friedman et al., 1999).

In addition to these factors that may exacerbate insulin resistance and impair glucose transport in pregnancy, there is evidence to suggest that the pathogenesis of GDM is contributed to by defects in the production and secretion of insulin by the β-cells (Lain...
Comparing pre-hepatic insulin secretion rates of women with GDM and matched non-diabetic pregnant controls, those women with GDM had a reduced insulin secretion rate in response to moderate hyperglycaemia in late pregnancy. This made it impossible for these women to compensate for their increased insulin resistance when compared with the non-diabetic control women (Homko, Sivan, Chen, Reece, & Boden, 2001). Other researchers have also shown that the rate of production of insulin for immediate release in response to a glucose load is lower in women with GDM, compared with pregnant women with normal glucose tolerance, despite higher overall insulin secretion levels in the GDM women (Kautzky-Willer et al., 1997). As such, the severity of a woman’s GDM should be assessed on both the extent of insulin resistance, and her ability to secrete insulin in response to a glucose load. Of interest, regular exercise may influence some of the factors addressed above.

1.6 Risk factors for developing GDM

As with most medical conditions, there are certain physiological and behavioural factors that increase the risk of developing GDM. While some factors such as genetic predisposition, maternal age and ethnicity cannot be changed, other lifestyle factors can be altered to help reduce the chance of developing the condition.

1.6.1 Non modifiable risk factors

Maternal age is a major risk factor for the development of GDM (Foster-Powell & Cheung, 1998; McGuire, Rauh, Mueller, & Hickock, 1996). Women over 35 years of age are at greater risk of GDM compared with younger women (Ferrara, Kahn, Quesenberry, Riley, & Hedderson, 2004). Indeed, the first Australian national report on the incidence of GDM reported a GDM prevalence of 1% in pregnant women aged 15-
19 years old compared with 13% of women aged 44-49 years of age (Templeton & Pieris-Caldwell, 2008). This is of concern given the increasing average maternal age in Australia from a mean of 28.1 years of age in 1992 (Lancaster, Pedisich, & Huang, 1995) to a mean of 30.1 years of age in 2012 (Hilder, Zhichao, Parker, Jahan, & Chambers, 2014).

Ethnicity is another non-modifiable risk factor for GDM, with women of non-Caucasian ethnicity having increased risk of GDM (Carolan, Davey, Biro, & Kealy, 2012). While it is uncertain if this is related to genetics or cultural habits; it is clear from retrospective and prospective surveys that the incidence of GDM is higher in women of Hispanic and Asian descent compared with non-Hispanic Caucasian women (Hedderson, Gunderson, & Ferrara, 2010). In a cohort study of approximately 220,000 women assessed over nine years (1995-2004), the age-adjusted prevalence of GDM was highest among Asian Indians, Filipinas and Southeast Asians (Hedderson et al., 2010). Furthermore, a prospective survey of women at the Saskatoon Royal University Hospital, Canada, between January to July 1998 recorded overall rates of GDM to be 3.5% for women of non-aboriginal descent compared with 11.5% for Aboriginal women (Dyck, Klomp, Tan, Turnell, & Doctor, 2002). Of note, the authors reported pre-gravid body mass index (BMI) (≥ 27 kg/m²) and maternal age (≥ 33 years) as the most important risk factors for GDM in Aboriginal women, whereas GDM in a previous pregnancy, family history of diabetes, and maternal age (≥ 38 years) were the strongest predictors for GDM in non-aboriginal women. Collectively, the aforementioned statistics highlight the elevated risk of GDM in non-caucasian women.
In addition to age and ethnicity, certain medical conditions may predispose a woman to GDM. In particular, polycystic ovarian syndrome (PCOS) is one of the most common female endocrine disorders affecting 5 - 10% of women in their reproductive years (Hart, Hickey, & Franks, 2004; Norman, Davies, Lord, & Moran, 2002). Diagnostic criteria for PCOS include the presentation of one or more symptoms of disturbance to the menstrual cycle, hyperandrogenism, insulin resistance and obesity (Hart et al., 2004). Since there is an inclination for women with PCOS to develop insulin resistance, it is not surprising that women with PCOS are reported to have an increased risk of developing GDM during pregnancy (Lo, Feigenbaum, Escobar, Yang, & et al., 2006; Mikola, Hiilesmaa, Halttunen, Suhonen, & Tiitinen, 2001). There is also some evidence to suggest that approximately 10% of GDM cases arise from existing genetic issues that result in an autoimmune or human leucocyte antigen-related condition (Lapolla, Dalfrà, & Fedele, 2009). In addition, as GDM bears similarities to other forms of diabetes, any genetic risk factors of type 1 and type 2 diabetes could also affect the risk of developing GDM (Petry, 2010).

Lastly, a previous history of GDM is one of the most predictive factors that determine the likelihood of recurring GDM. In a meta-analysis on 13 studies published between 1977 to 2002 on GDM recurrence, the recurrence rates ranged from 30% to as high as 84% depending largely on the ethnicity mix of the study cohort (Kim, Berger, & Chamany, 2007). Specifically in Australia, 480 women with GDM were studied over a 5-year period from 1990 to 1994 (Moses, 1996). Within the study period, one-fifth of women had subsequent pregnancy and 35% of these women were diagnosed with GDM. A separate retrospective review of 540 Australian women with GDM in New South Wales from 1990 to 1996 reported a GDM recurrence rate of 62% (Foster-Powell...
More recently, others have reported a 38% risk of GDM in American women with a history of the condition, compared with an age-adjusted risk of 3.5% in the second pregnancy of women who did not previously have GDM (Ehrlich et al., 2011). The high risk of GDM recurrence is likely contributed to by multiple factors such as advancing maternal age. However, it is important to note that the modifiable risk factors for GDM (outlined below) are often exacerbated in women experiencing subsequent pregnancies, with the potential for greater weight retention postpartum and more barriers to physical activity due to increased household responsibilities associated with caring for other children.

1.6.2 Modifiable risk factors

While maternal age, family and medical history cannot be altered, there are a number of lifestyle and behavioral factors that can be modified in order to reduce the risk of developing GDM. In relation to nutrition, there is increasing evidence that a lack of vitamin D is associated with glucose intolerance in pregnant women (Lau, Gunton, Athayde, Byth, & Cheung, 2011; Maghbooli, Hossein-nezhad, Karimi, Shafaei, & Larijani, 2008; C. Zhang et al., 2008). However, more research is required to determine if increasing vitamin D levels in the body via supplementation can reduce the risk of GDM. Additionally, there is increasing research on the use of probiotic supplementation to reduce the occurrence of GDM (Barrett, Dekker, & Callaway, 2014). For instance, one randomised controlled trial reported a 60% reduction in GDM incidence in women who took probiotics from early pregnancy compared with women who were given a placebo or dietary intervention (Laitinen, Poussa, & Isolauri, 2008).
Another modifiable risk factor for GDM is a woman’s pre-pregnancy body mass, which may be altered with diet and exercise. Indeed, overweight women are twice as likely to develop GDM as normal weight women (Chu et al., 2007). The risk becomes 3.5 fold higher if obese; and 8.5 fold higher if morbidly obese compared with normal-weight women (Chu et al., 2007). This is related, in part, to the fact that both obesity and pregnancy contribute independently to an increase in insulin resistance in the body, with both adipose tissue and the placenta functioning as an endocrine organ and secreting hormones that regulate maternal metabolism (Power & Schulkin, 2012). Of relevance, the natural resistance to insulin brought about by placental hormones can be worsened by adipokines released by the adipose tissue (Power & Schulkin, 2012).

In addition to pre-pregnancy body mass, excessive rates of gestational weight gain during pregnancy, especially during the early stages of gestation, appears to increase a woman’s risk of GDM (Hedderson et al., 2010). In particular, gestational weight gain is a significant risk factor for GDM in women who are already overweight or obese (Gibson, Waters, & Catalano, 2012). According to the Institute of Medicine (IOM) guidelines, the current recommended weight gain during pregnancy for overweight women (BMI 25.0 - 29.9 kg/m²) is 6.8 – 11.3 kg; and for obese women (BMI ≥ 30 kg/m²) is 5.0 – 9.1 kg (Rasmussen & Yaktine, 2009). Therefore, if it is not possible to reduce body mass to the healthy range before falling pregnant, minimising excessive weight gain during pregnancy may help with risk reduction.

Physical inactivity is another modifiable risk factor for GDM. Indeed, physical inactivity is also one of the contributing factors for maternal overweight and obesity (Bryan & Walsh, 2004; Sugiyama, Healy, Dunstan, Salmon, & Owen, 2008). This is of
concern given that being overweight or obese and physically inactive occurs in a large proportion of women with existing children and incidentally also causes a higher prevalence of GDM in women of childbearing age (Petersen, Leet, & Brownson, 2005; Poudevigne & O’Connor, 2006; Simmons, 2011). Engaging in regular physical activity can prevent excessive weight gain during pregnancy (Streuling et al., 2011; Stuebe, Oken & Gillman, 2009). In contrast, women who do not meet physical activity guidelines during pregnancy have been reported to be more likely to exceed IOM guidelines for gestational weight gain (Kraschnewski et al., 2013). However, physical inactivity is also an independent risk factor for the development of GDM. Importantly, epidemiological studies have indicated that being physically active before and during pregnancy is associated with reduced risk of GDM (Dempsey, Butler, & Williams, 2005; Dempsey, Sorensen, et al., 2004). In a meta-analysis of eight studies, Tobias, Zhang, van Dam, Bowers, and Hu (2011) found that greater total physical activity before and during pregnancy were significantly associated with a reduced risk of GDM. Collectively, this epidemiological evidence suggests that being physical active before and during pregnancy may prevent or reduce the risk of GDM. The role of exercise in GDM prevention will be discussed in further detail in Sections 1.13 and 1.14.

1.7 Screening & Diagnosis of GDM

In Australia, two methods are employed for the screening and diagnosis of GDM. Traditionally, pregnant women who are not considered at high risk of GDM undergo a Glucose Challenge Test (GCT) to screen for abnormal glucose tolerance. Over the years, the GCT, while still in use by some medical practitioners, has largely been abandoned by most as it does not require women to fast prior to blood sampling which may result in inaccurate diagnosis and subsequently, additional GDM blood screening.
As such, while it was usual practice for only women who are at high risk of GDM to undergo an oral glucose tolerance test (OGTT) directly, most practitioners now require all pregnant women, both low and high risk, to undergo an OGTT. Of note, women who meet one or more of the following criteria are considered at high risk of GDM. These criteria include; a previous history of GDM, being of non-caucasian ethnicity, having a maternal age ≥ 40 years, a family history of diabetes, a BMI ≥ 35 kg/m² or women with PCOS.

Of relevance, the GCT involves the ingestion of a solution containing 50 g of glucose. One hour later, a venous blood sample is collected from an antecubital vein and analysed for blood glucose levels (BGL). A 1-hour BGL of less than 7.8 mmol/L indicates that GDM is unlikely. In contrast, women with an abnormal GCT result (i.e. 1-hour blood glucose ≥ 7.8 mmol/L) are requested to undergo an OGTT on a separate occasion to confirm a diagnosis of GDM and to determine the severity of glucose intolerance. An OGTT requires an overnight fast, followed by the ingestion of a 75 g glucose solution the next morning. Venous blood samples are collected once before and twice after the ingestion of the glucose drink (at 1 and 2 h post). Prior to 2012, the cut off values for diagnosing GDM following an OGTT were a fasting venous plasma glucose (PG) of ≥ 5.5 mmol/L and/or a 2-h venous PG ≥ 8.0 mmol/L. However, in 2012, the Australasian Diabetes in Pregnancy Society issued new guidelines for the diagnosis of GDM. These included a fasting venous PG of ≥ 5.1 mmol/L; 1-h venous PG ≥ 10.0 mmol/L; and/or a 2-h venous PG ≥ 8.5 mmol/L (Nankervis et al., 2012). Reaching one of these three thresholds confirms a diagnosis of GDM. Of note, the new ADIPS guidelines are adopted by some, but not all medical providers in Australia due to opposing viewpoints regarding the methodology involved in deriving the cutoff values.
1.8 Prevalence of GDM

Currently GDM affects 1% to 14% of pregnant women around the world (Bottalico, 2007). The large discrepancy in prevalence is due to the different populations examined and the varying diagnostic criteria employed (Bottalico, 2007). Regardless of the disparity in screening methods, there is an overall increasing trend of GDM prevalence globally, particularly in European countries (Buckley et al., 2012), as well as the United States of America, Australia (Templeton & Pieris-Caldwell, 2008) and South East Asian countries including India (Seshiah, Balaji, Balaji, Sanjeevi, & Green, 2004) and China (Zhang et al., 2011). According to the first national report on the incidence of GDM in Australia (Australia Institute of Health and Welfare; AIHW, 2010), diagnosis of the condition had increased by 22% over a six year period between 2000-2001 and 2005-2006. From 2007 to 2008, it was further estimated that 5% of women who gave birth at a hospital had GDM (AIHW, 2010). A more recent survey of the global prevalence of GDM reported Australia to have a GDM prevalence rate of 6 – 9% (Jiwani et al., 2012). With increasing prevalence of diabetes risk factors such as overweight/obesity and physical inactivity worldwide, it is not surprising that GDM recurrence can be as high as 45 - 69% in some populations (Ben-Haroush, Yoge, & Hod, 2004; Kwak et al., 2008). At this rate of increase, the incidence of GDM is adding burden to health care systems globally because of the health implications of the condition for mother and her child.

1.9 Health implications of GDM for the woman

The immediate health implications faced by a woman diagnosed with GDM include increased risk of pre-eclampsia, infection, and postpartum haemorrhage (Dempsey et al., 2005). As prolonged exposure to excessive levels of glucose in the intrauterine
environment increases the probability of developing a macrosomic baby (birthweight of 4000 g or more), women with GDM are at higher risk of uterine rupture and perianal lacerations during labour (Jastrow et al., 2010). Compared with non-diabetic women, pregnancies of diabetic women also have increased rates of intrauterine death, perinatal morbidity and mortality (Miller & Gillmer, 2005; Xiong, Saunders, Wang, & Demianczuk, 2001). As such, the birth plan for delivery in women with GDM is usually either induced labour or elective caesarean section in order to minimise the occurrence of emergency surgical interventions and to avoid the associated risk with birth trauma and other complications (National Collaborating Centre for Women’s and Children’s Health, 2008). Unfortunately, these medical interventions also pose risk to the woman due to the possibility of excessive blood loss, respiratory complications as a result of anaesthesia, infection, as well as the potential increased need for additional surgeries (Bloom et al., 2005; Miller Jr, 1988; Petitti, 1985; Shearer, 1993).

In the longer term, although the hyperglycaemic state of GDM usually resolves itself naturally postpartum, the woman has increased risk of another GDM diagnosis in subsequent pregnancies (Ben-Haroush et al., 2003). The independent risk factors of recurrence include higher pre-pregnancy BMI, lower 1-h insulin concentration in an OGTT during gestation and higher fasting glucose levels in an OGTT conducted two months postpartum (Kwak et al., 2008). Furthermore, the overall frequency of GDM diagnosis in a woman’s life contributes to the risk of her developing type 2 diabetes in the future. Indeed, a mother experiencing GDM in her pregnancy has a higher tendency of developing type 2 diabetes mellitus within five years of delivery (Kim, Newton, & Knopp, 2002). Some estimates suggest that women with GDM are six times more likely to develop type 2 diabetes later in life compared with women with normal glucose
tolerance during pregnancy (Cheung & Byth, 2003). The likelihood of developing type 2 diabetes is predictable, at least in part, by the extent of hyperglycemia observed in an OGTT during pregnancy; pre-pregnancy BMI; as well as by factors such as persistent fasting hyperglycemia in GDM; the need for insulin therapy or repeated diagnosis of GDM in subsequent pregnancies (Aberg, Jonsson, Eskilsson, Landin-Olsson, & Frid, 2002; Cheung & Helmink, 2006; Foster-Powell & Cheung, 1998). Since type 2 diabetes is associated with numerous chronic health complications including heart disease and stroke, kidney disease and failure, retinopathy, neuropathy, skin and foot complications (Deshpande, Harris-Hayes & Schootman, 2008), it is not surprising that GDM has major medical and socioeconomic implications for our community.

Another potential long-term implication for women with GDM may be an increased risk of future cardiovascular disease. Of relevance, a study reported that a previous diagnosis of GDM is associated with early subclinical atherosclerosis before the onset of diabetes and the metabolic syndrome regardless of pre-pregnancy obesity, race, parity, and age (Gunderson et al., 2014). In addition, women with a history of GDM have higher mean levels of cardiovascular disease markers (i.e. C-reactive protein, IL-6 and plasminogen activator inhibitor-1 which are indicative of subclinical inflammation) compared with women without prior GDM (Heitritter, Solomon, Mitchell, Skali-Ounis, & Seely, 2005). Furthermore, women with a history of GDM have been found to have increased peripheral vascular resistance, which is a potential indicator of early vascular dysfunction (Heitritter et al., 2005).
1.10 Health implications of GDM for the offspring

There are also several serious health risks for the offspring of women diagnosed with GDM. For example, the elevated maternal glucose concentration available to the fetus promotes increased fetal insulin secretion, excessive growth, and macrosomia (Persson, Eriksson, & Hanson, 2005). This often results in a difficult labour and injury during birth because the excessive growth occurs disproportionately, favouring growth of the shoulders rather than the head, leading to a predisposition to shoulder dystocia, surgical intervention and increased rates of admission to a neonatal care unit (Andreasen, Andersen, & Schantz, 2004). In contrast to excessive growth in the fetus, chronically high levels of glucose in the fetus in severe and untreated GDM cases can also lead to fetal growth restriction, as the fetal supply of nutrients and oxygen is compromised due to fetal hypoxia and hyperinsulinaemia associated with chronic hyperglycemia (Persson et al., 2005).

Persistent elevated levels of circulating insulin in response to the hyperglycaemia experienced in the intrauterine environment can also cause a newborn to experience hypoglycaemia at birth, presenting symptoms such as jitteriness, a weak or high-pitched cry, floppiness or lethargy and poor feeding (Adamkin, 2011). A prolonged state of hypoglycemia in an infant may also lead to comas and seizures (Adamkin, 2011). As such, the management of hypoglycemic infants presenting the aforementioned symptoms and a blood glucose level of less than 2.2 mmol/L involve immediate intravenous glucose treatment, or in less serious cases, an increased frequency of feeding to return infant blood glucose levels to normative concentrations (Kalhan & Peter-Wohl, 2000).
A child born from a pregnancy complicated by GDM also has lifelong health risks. For example, macrosomic infants are at increased risk of being obese and/or suffering from type 2 diabetes and metabolic syndrome in later life (Boney, Verma, Tucker, & Vohr, 2005; Lauemborg, Mathiesen, & Damm, 2005; Wang et al., 2009; Eriksson, Forsen, Osmond, & Barker, 2003). Further, children born to mothers with GDM are at increased risk of cardio-metabolic disorders. In a study of 164 Chinese children of women with and without GDM (Tam et al., 2008), those children exposed to maternal GDM had significantly higher blood pressure and lower high-density lipoprotein cholesterol levels, after adjustment for age and gender (Tam et al., 2008).

1.11 Management of GDM

Overall, the increased health risks for a mother and child from a pregnancy complicated by poorly controlled GDM represents one of the gravest future health problems in our community as the long term outcome may result in perpetuating serious health consequences in subsequent generations (Huang et al., 2006; Newnham, Pennell, Lye, Rampono, & Challis, 2009). As such, several strategies are implemented in an attempt to effectively manage GDM when diagnosed.

Nutritional education is the initial strategy employed for the management of GDM. This mode of management is usually referred to as medical nutrition therapy (MNT) (Metzger, 2006). Medical nutrition therapy aims to ensure sufficient nutrition for the mother and her growing fetus, and to promote desirable levels of gestational weight gain, whilst maintaining normal blood glucose levels and avoiding a state of ketosis (Franz et al., 2002). In Australia, women diagnosed with GDM are commonly referred to a dietitian who determines their nutritional requirements on an individual basis in
order to maintain optimum blood glucose levels. The efficiency of MNT in maintaining appropriate glucose concentrations in the blood is confirmed by regular self-monitoring of fasting and postprandial measurements. If daily capillary monitoring of glucose concentrations shows a lack of glycemic control after two weeks of MNT (i.e. consistent daily fasting/pre-prandial BGL > 5.5 mmol/L or 1-hr post prandial BGL > 7.0 mmol/L), insulin therapy or the oral hypoglycemic agent metformin may be considered.

Of note, pregnant women with GDM, whether treated by MNT or by insulin therapy, are encouraged to engage in 30 min of moderate exercise each day as an adjunct therapy for glycaemic control. This prescription is based on several studies showing the effectiveness of exercise for the management of blood glucose levels in women with GDM (Avery & Walker, 2001; Brankston, Mitchell, Ryan, & Okun, 2004; Davenport, Mottola, McManus, & Gratton, 2008; de Barros, Lopes, Francisco, Sapienza, & Zugaib, 2010; García-Patterson et al., 2001; Halse, Wallman, Newnham, & Guelfi, 2014; Jovanovic-Peterson & Peterson, 1991). Although exercise is widely recommended as a management tool for GDM, whether regular exercise per se is successful at preventing the condition from manifesting in the first place is yet to be confirmed.

1.12 Is exercise safe during pregnancy?

Before suggesting exercise as a possible strategy to prevent GDM, the safety of exercise in pregnancy should be discussed. The belief that maternal exercise represents a risk for fetal growth and development is still held by many in society. While excessive and overly intense exercise during pregnancy can be harmful, there is no evidence that regular moderate intensity exercise performed is detrimental to the fetus (Clapp, 1996;
Clapp, Lopez, & Harcar-Sevcik, 1999). In fact, babies born to women who exercised regularly showed no growth or development delay at one and five years of age (Clapp, 1996; Clapp, Simonian, Lopez, Appleby-Wineberg, & Harcar-Sevcik, 1998). However, more studies need to be conducted to affirm the effects of maternal exercise during pregnancy on the long term health outcomes of their offspring. Indeed, a meta-analysis of 18 studies of exercise in pregnancy concluded that a moderate intensity exercise program comprising of different exercise modes, performed three times a week (mean duration: 43 min) was not associated with adverse effects to the mother or fetus in a healthy normal pregnancy (Lokey, Tran, Wells, Myers, & Tran, 1991). The safety of exercise for the maternal-fetal unit has been further confirmed in many studies, even when the intensity is vigorous enough to promote cardiovascular improvements during pregnancy, with no adverse effects reported in infants of exercising women in terms of overall length of pregnancy, fetal birth weight, Apgar scores or placental weight compared with inactive controls (Halse, Wallman, Dimmock, Newnham, & Guelfi, 2015; Price, Amini, & Kappeler, 2012). Other researchers have also reported that moderate intensity exercise has no negative effects on labour outcomes or neonatal condition (Melzer, Schutz, Soehnchen, et al., 2010). However, appropriate precautions are required when prescribing exercise in pregnancy. Of note, exercise is not recommended for women with pregnancy complications such as evidence of intrauterine growth restrictions, uncontrolled type 1 diabetes, hypertension or thyroid diseases, or persistent bleeding in the second and third trimesters (Wolfe & Mottola, 2002).
1.13 Effects of regular exercise on glucose tolerance and insulin sensitivity in pregnancy

In addition to the existing research that supports the safety of exercise in healthy pregnancies, exercise may be beneficial for attenuating the natural decline in glucose tolerance and insulin sensitivity observed during pregnancy. For example, our research group has shown that a 10-week fully supervised, home-based exercise program (three sessions per week of stationary cycling, commenced at 18 weeks of gestation) attenuates the decline in glucose tolerance in obese pregnant women (Ong et al., 2009). Likewise, Callaway and colleagues (2010) reported a trend for improved fasting glucose levels at 28 weeks of pregnancy in obese women who engaged in an individualised exercise program (from 12-40 weeks gestation). In contrast, two studies showed that regular exercise had no effect on maternal glycemic control or insulin sensitivity (Hopkins, Baldi, Cutfield, McCowan, & Hofman, 2010; Oostdam et al., 2012). In the study by Hopkins and colleagues (2012), a home-based stationary cycling intervention commenced at 20 weeks of gestation through to delivery, performed to a maximum of five sessions a week for 40 minutes/session resulted in changes to offspring size without changes in maternal insulin sensitivity. Similarly, no change in fasting maternal glucose levels or insulin sensitivity was observed after a program of aerobic and resistance training commenced around 15 weeks of pregnancy (two-session per week for 60 min) (Oostdam et al., 2012). However, it is important to note that only 16.3% of participants were compliant to the exercise intervention in the study by Oostdam and colleagues, compared with 94% and 73% in the studies by Ong and colleagues (Ong et al., 2009) and Callaway and co-workers (Callaway et al., 2010), respectively. However, the study by Hopkins and colleagues (2010) reported a compliance rate of 75%,
suggesting that there may be other factors that influence the effect of regular exercise on glucose tolerance and maternal insulin sensitivity.

Still, the importance of compliance to an exercise intervention is crucial to effectively assess the effect of regular exercise on glucose tolerance and maternal insulin sensitivity. This may be highlighted in a more recent randomised controlled trial investigating the effects of maternal exercise on glucose tolerance (Barakat, Cordero, Coteron, Luaces, & Montejo, 2012). This study involved an exercise group (EG; n = 40) that engaged in three instructor-led sessions of exercise per week (either land or aquatic) commenced at 6-9 weeks of pregnancy and a control group (CG; n = 43) which did not receive the exercise intervention. With a high compliance rate of 85% to the exercise intervention, these researchers reported that women in the exercise group had improved maternal glucose tolerance at 24-28 weeks of pregnancy compared with women in the control group.

Based on these potential benefits of regular exercise for glucose tolerance in a pregnant population, larger randomised controlled trials with exercise interventions that encourage optimal adherence are required to assess the effect of exercise on the incidence of GDM. It would also be beneficial to monitor and standardise the level of intensity of the intervention to determine the exact exercise prescription required for preventing GDM.

1.14 Prevention of GDM through regular exercise

The previously mentioned evidence to support a beneficial effect of exercise on glycemic control in pregnancy suggest that the use of regular exercise as a prevention
strategy for GDM is worthy of investigation. Epidemiological studies support a potential role of exercise for preventing GDM (Mudd, Owe, Mottola & Pivarnik, 2013). Based on retrospective data from a population-based birth registry, obese women who reported higher levels of exercise during pregnancy were 47% less likely to be diagnosed with GDM than women who did not exercise (Dye, Knox, Artal, Aubry, & Wojtowycz, 1997). Furthermore, Dempsey and colleagues (2004) collected data on self-reported physical activity levels a year prior to pregnancy, as well as in early gestation from normotensive, non-diabetic women (n = 909). They found that women who participated in any recreational activity both before and during pregnancy had a reduced rate of subsequent diagnosis of GDM. While the type of activity was not specified, the greater the number of hours spent performing recreational activity before and during pregnancy, the greater the reduction in risk of developing GDM [any amount of physical activity, 56% risk reduction (RR = 0.44, 95% CI: 0.21, 0.91; ≥ 4.2 hours/week of physical activity, 76% risk reduction (RR = 0.24, 95% CI: 0.10, 0.64)]. Additionally, a case-control study by the same authors found that regular maternal physical activity in the first 20 weeks of pregnancy was associated with an approximate halving of the risk of GDM (Dempsey, Butler, et al., 2004).

Based on these trends reported by epidemiological studies, randomised controlled studies investigating the role of regular exercise in preventing GDM have begun to emerge over the last few years. To the authors’ knowledge, there are five published randomised controlled trials on the role of exercise in the prevention of GDM with conflicting outcomes (Barakat, Pelaez, Lopez, Lucia, & Ruiz, 2013; Cordero, Mottola, Vargas, Blanco, & Barakat, 2014; Koivusalo et al., 2015; Nobles et al., 2015; Stafne et al., 2012) and one other randomised controlled trial that reported incidence of GDM as a
secondary measure (Price et al., 2012). The first study allocated 855 women to either a 12-week standard exercise program or standard antenatal care commencing at 18-22 weeks of gestation (Stafne et al., 2012). Their intervention program included one group exercise training session per week led by a physiotherapist [60-min duration; intensity measured by rate of perceived exertion (RPE) 13-14], in addition to two 45-min unsupervised home exercise sessions during the week. All sessions included both aerobic and body weight resistance exercises that targeted the upper and lower limbs, back extensors, deep abdominal and pelvic floor muscles. Contrary to epidemiological data, these researchers found no significant differences in the incidence of GDM between the group that received the 12-week exercise program and the group that received standard antenatal care. However, it is important to note that adherence to the exercise program in this study was only 55%. As such, the authors conducted an explorative analysis on protocol-adherent women who exercised three times a week or more, at a moderate to high intensity. It was found those participants who adhered to the exercise program had significantly lower fasting insulin levels and insulin resistance at follow up compared with the control group who received standard care (Stafne et al., 2012). It is also possible that an exercise intervention commencing at 18-22 weeks of gestation may provide limited benefits for GDM prevention compared with an intervention starting earlier in gestation, given that GDM normally manifests at 24-28 weeks of gestation.

The second randomised controlled trial utilised a similar exercise intervention to Stafne and colleagues (2012). Bakarat and colleagues (2013) randomised 510 healthy pregnant women into an exercise intervention group or a control group who received routine care plus physical activity advice (n = 255, each). The exercise program commenced from 10
to 12 weeks of pregnancy and focused on moderate-intensity resistance and aerobic exercises (three times/week, 50–55 min/session). This study reported that the exercise intervention did not reduce the risk of developing GDM, even though their exercise compliance rate was > 95%. Of note, the participants of this study underwent their OGTT between 24-26 weeks of gestation when pregnant women were routinely tested at 28 weeks of gestation. Furthermore, the physical activity levels of women in the control group (that was provided with physical activity advice) were not monitored. Whilst the participants in the control group all reported not engaging in any regular physical activity program for more than 20 min or more than 3 days/week, there is no certainty that the physical activity and dietary behaviour of the control group were not altered as a result of joining the study.

The third randomised controlled trial involved a sample of 272 pregnant women, of which less than 5% of participants had a history of GDM (Cordero, Mottola, Vargas, Blanco & Barakat, 2014). Their intervention group (n = 101) performed moderate intensity exercise three times a week for 50-60 min (land and aquatic activity) and their control group (n = 156) received standard care. Gestational diabetes was diagnosed in 1% of participants in the intervention group and 8.8% in the control group (p = 0.009) suggesting that engaging in the exercise program during pregnancy reduced the incidence of GDM. The results from these study suggest a frequency of at least three times per week of exercise which involves a mixture of aerobic and muscle conditioning exercise, on land and in water (for 50 min; an intensity of 60% predicted HR reserve; RPE 12–14, equivalent to ‘somewhat hard’ on Borg’s scale), may reduce the incidence of GDM women without a history of the condition.
The two most recent randomised controlled trials (Koivusalo et al., 2015; Nobles et al., 2015) had an overall goal of encouraging pregnant women to achieve the recommended levels of physical activity during pregnancy rather than implementing a structured exercise intervention. Nobles and colleagues (2015) found no effect on GDM incidence, perhaps as a result of the intervention commencing later in pregnancy (at 18 ± 4 weeks gestation). However, Koivusalo and colleagues (2015) found a positive impact of their exercise intervention on the incidence of GDM (intervention group, 13.9%; control group, 21.6% [95% CI 0.40–0.98%] P = 0.044). Of note, none of these studies focused on preventing GDM in women who were diagnosed with GDM in a previous pregnancy - a group at the highest risk of this condition. Future research is needed to address this issue, as well as to enhance the design of exercise interventions to ensure optimal compliance.

1.15 Additional benefits of exercise during pregnancy

Regardless of whether regular exercise can prevent GDM, exercise during pregnancy provides other physiological and psychological benefits to both the mother and her child.

1.15.1 Benefits of exercise for the pregnant woman

Regular moderate intensity aerobic exercise during pregnancy has positive effects on maternal aerobic fitness. Women who engage in aerobic exercise throughout pregnancy have lower resting heart rates and higher stroke volumes (i.e. better cardiovascular fitness) when compared with matched sedentary pregnant women (Melzer, Schutz, Boulvain, & Kayser, 2010; O'Toole, 2003). In addition, exercising throughout pregnancy has been associated with beneficial effects for achieving greater levels of fitness and reduced cardiovascular risk factors later in life (Clapp, 2008). Several
intervention-based studies have also reported significant improvements in physical fitness in previously sedentary women who exercised regularly (≥ 3 times a week and/or ≥ 30 min/per session) during pregnancy (Collings, Curet, & Mullin, 1983; Marquez-Sterling, Perry, Kaplan, Halberstein, & Signorile, 2000; Prevedel, Calderon, De Conti, Consonni, & Rudge, 2003; Price et al., 2012; Santos et al., 2005). For instance, Santos and colleagues (2005) reported that performing three one-hour sessions of aerobic exercise each week (for 12 weeks) could increase oxygen uptake at the anaerobic threshold by 18% in overweight women, while a 16% decrease was seen in their control group compared with their baseline levels (17-18 weeks gestation). Further, in a recent randomised controlled trial, sedentary women were allocated into either an exercise group (45-60 min of aerobic exercise, four times a week; three supervised sessions and one self-conducted walking session; n = 31) or a control group (n = 31) at 12-14 weeks of pregnancy (Price et al., 2012). These researchers showed that women in the exercise group significantly improved aerobic fitness and muscular strength compared with sedentary controls by 30-32 weeks of pregnancy. Of importance, the studies by Santos et al (2005) and Price et al (2012) are evidence that exercise interventions involving durations between 45 to 60 min are feasible in women with low-risk pregnancies who have been previously sedentary. Precautionary considerations should be made in terms of the each woman’s pre-pregnancy BMI and the relationship of intensity and duration of exercise.

Another benefit of exercise during pregnancy is a reduction in maternal physical discomforts. Most women suffer some form of physical discomfort during gestation as the maternal musculoskeletal system changes to accommodate the growing fetus. Increased laxity and hypermobility in certain joints during pregnancy commonly leads
to pelvic and lower back pain (Artal & O'Toole, 2003) and these conditions are experienced by 50-72% of pregnant women (Mogren & Pohjanen, 2005). Of relevance, back pain has been cited as the most commonly reported reason for sick leave from work during pregnancy (Ostgaard & Andersson, 1992). Importantly, some studies report that women who exercise during pregnancy experience less severe back pain than those who do not exercise (Garshasbi & Faghih Zadeh, 2005; Kihlstrand, Stenman, Nilsson, & Axelsson, 1999). Specifically, researchers found that lower back pain was significantly reduced in women who performed water aerobics once a week for an hour in the second half of pregnancy, compared with those who did not (Kihlstrand et al., 1999). Similarly, women who engaged in a 12-week exercise program during the second half of pregnancy (60 min consisting of 15 strengthening and stretching exercises) showed significant reductions in lower back pain intensity compared with a control group of women who did not engage in the exercise program (Garshasbi & Faghih Zadeh, 2005).

Pregnant women may also experience other physical discomforts such as oedema in the legs (Katz, 2003) and leg cramps (Koniak-Griffin, 1994), which in turn may contribute to decreased mobility. Research has shown that women who participated in a 6-week aquatic exercise program (3 x 1-hr sessions per week) not only experienced reduced overall maternal discomfort, but also had improved mobility compared with women who continued their normal activities of daily living (Smith & Michel, 2006).

The advantages of regular exercise during pregnancy extend to the psychological domain, with exercise reported to improve body image, self-esteem (Hall & Kaufmann, 1987; Wallace, Boyer, Dan, & Holm, 1986), mental health and quality of life during
pregnancy (Smith & Michel, 2006). The aforementioned psychological benefits of exercise are important given that amidst the discomforts of pregnancy, a woman is also undergoing a state of vulnerability in her mental status (Artal, Wiswell, & Drinkwater, 1991). Furthermore, negative mood states are strongly linked to perceived stress, which in turn, is associated with a variety of negative outcomes for the mother and her child (Lederman, 1995). In addition to the normal fluctuation of mood states, women have a higher chance of experiencing clinical depression or anxiety in the months leading up to delivery and postpartum (Pivarnik et al., 2006).

Exercise may also improve a woman’s perception of health which may impact overall psychological wellbeing. In a recent randomised controlled trial on the effects of exercise on maternal health perceptions (n = 80), participants either engaged in a thrice weekly program of aerobic and resistance exercises at a moderate intensity (≤ 70% age predicted heart rate) for 35-45 min per session; or they did not (Barakat, Pelaez, Montejo, Luaces, & Zakynthinaki, 2011). The exercise intervention began at 6-9 weeks of pregnancy and continued until 38-39 weeks gestation. Women in the exercise group showed significant increases in their perception of personal health status compared with women in the control group (Barakat et al., 2011). This improvement in self-perceived health status could benefit the overall sense of wellbeing for the pregnant woman.

Lastly, engaging in exercise during pregnancy may have some benefit for the mother’s labour and delivery process, as well as her risk of caesarean delivery (Katz, Kroll, Shapiro, Cristal, & Meizner, 1990). Oxygen uptake had been recorded at 0.338 L/min during contractions at 4 cm dilation and 0.510 L/min at delivery in healthy pregnant women which indicate labour as an aerobic process (Katz et al., 1990). Therefore,
having better cardiovascular fitness may have positive outcomes for the process of childbirth (Katz et al., 1990). In a study on the association between aerobic fitness in late pregnancy and the duration of labour, 40 nulliparous women underwent a maximal oxygen update test late in gestation (35-37 weeks) and had their labour time recorded (Kardel, Johansen, Voldner, Iversen, & Henriksen, 2009). Data, adjusted by birth weight, showed that the duration of labour was inversely related to maximal oxygen uptake, suggesting that women with greater aerobic fitness have a shorter duration of spontaneous labour (Kardel et al., 2009). Similarly, Beckmann and Beckmann (1990) reported that physically conditioned women had significantly shorter first and second stages of labour than women who did not exercise. Furthermore, women who were physically active in the first and second trimester have been reported to have reduced risk of experiencing a caesarean section during labour (Bungum, Peaslee, Jackson, & Perez, 2000). However, given the uniqueness of each pregnancy, some studies have also reported no effects of exercise on labour duration, and medical intervention rates (Collings, Curet, & Mullin, 1983; Thangaratinam et al., 2012)

1.15.2 Fetal & neonatal benefits of exercise during pregnancy

Research has indicated that there may be cardiovascular benefits arising from performing exercise during pregnancy for the offspring; both during gestation as well as after birth. For example, the fetal cardiovascular system does, in fact, respond to maternal exercise (Collings et al., 1983; Cooper, Hunyor, Boyce, O’Neill, & Frewin, 1987; Lotgering, Gilbert, & Longo, 1985) indicating possible adaptions to an exercise stimuli for the fetal physiological system. Transient periods of reduced uterine blood flow appear to stimulate physiological benefits for placental growth and function, which in turn may have positive effects on fetal behaviour (Clapp & Capeless, 1997; Clapp &
Rizk, 1992; Hatoum, Clapp, Newman, Dajani, & Amini, 1997). Although there is limited literature on the effects of maternal exercise on a fetus’ cardiovascular system, a study on regular exercisers (≥ 30 min of aerobic exercise, 3 session/week) (n = 26) and non-exercisers (n = 35) during pregnancy, found that the fetal heart rate of pregnant exercisers was significantly lower than those who did not exercise (May, Glaros, Yeh, Clapp, & Gustafson, 2010). In addition, higher heart rate variability, which is considered to be a positive indicator of fetal wellbeing (Samueloff et al., 1994), was observed in the fetus of women who exercised regularly. There is also some preliminary evidence for beneficial effects of maternal exercise on fetal cardiovascular responses in utero (May, Glaros, Yeh, Clapp & Gustafson, 2010) and after the fetus is born (May, Scholtz, Suminski & Gustafson, 2014). These researchers showed that regular maternal aerobic exercise during pregnancy was associated with lower fetal heart rate (HR) and higher heart rate variability (HRV) at 36 weeks gestation and the increase in fetal cardiac autonomic control persisted a month after birth in infants born to women who were regular exercisers during pregnancy (3 times per week, ≥ 30 min of aerobic exercise) compared with infants of non-exercising women (May et al., 2010; May et al., 2014). Whether these benefits for the offspring last into adulthood remains to be determined.

A series of studies by Clapp and colleagues (1996 – 1999) provides further evidence of benefit of maternal exercise for the offspring. For example, babies born to women who exercise regularly have been shown to have lower body mass and less fat mass at birth and score significantly higher in the Brazelton Neonatal Behavioural Assessment Scale for their orientation behaviour and ability to settle themselves after exposure to external stimulus five days after delivery (Clapp et al., 1999). Furthermore, children of women
who exercised regularly in pregnancy weighed less and were leaner at five years of age compared with children of women who did not exercise regularly. The group of children born to women who exercised in pregnancy also tested significantly better on the Wechsler scale for intelligence and on tests of oral language skills compared to their counterparts at 5 years of age (Clapp, 1996). Of note, the women in all three of these studies participated in three or more sessions of aerobic-type exercise (such as running, aerobics or swimming) per week for more than 20 min at a time. The intensity of exercise was reported to be more than 55% of the maximal aerobic capacity.

1.16 Current physical activity recommendations during pregnancy

Given the numerous benefits of regular exercise during pregnancy, the American College of Obstetricians and Gynaecologists (ACOG) suggest that women without medical or obstetric complications should aim for an eventual goal of moderate-intensity exercise for at least 20–30 minutes per day on most or all days of the week, developed with the patient and adjusted as medically indicated (Artal & Hopkins, 2013; ACOG, 2015). More specifically, the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Canadian Society of Exercise Physiology (CSEP) recommend that pregnant women increase their duration of their exercise gradually to 30 minutes up to four times a week (Davies, Wolfe, Mottola, & MacKinnon, 2003).

1.16.1 Special considerations for exercise during pregnancy

While adhering to these guidelines, pregnant women should avoid hyperthermia during exercise (i.e. maintaining body temperature of 36.9°C). The risk of overheating is most critical in the first trimester of pregnancy as major cell divisions are occurring and an increase in core temperature of the mother could lead to fetal malformations (Edwards, 1986; Milunsky et al., 1993). Women should also avoid performing exercise in a supine...
position after the first trimester of pregnancy (i.e. performing sit ups or lying flat on the back). Exercising or lying in supine position pertains more to the late second and third trimesters as the weight of the fetus and placenta could restrict blood flow of the inferior vena cava and lead to a condition known as supine hypotension syndrome (Brigden, Howarth, & Sharpey-Schafer, 1950), which could reduce cardiac output, as well as blood pressure. In addition, activities that have a risk of loss of balance and fetal trauma should not be performed (Artal & O’Toole, 2003; Davis et al., 2003).

Pregnant women who engage in regular exercise should also be aware of appropriate nutrient replacement before and after exercise. Blood glucose concentrations decrease at a faster rate and to significantly lower levels post-exercise during pregnancy compared with non-pregnant women (Soultanakis, Artal, & Wiswell, 1996). While this decrease does not seem to cause low blood glucose after prolonged exercise (e.g. 40 min of moderate walking or aerobic dancing) (Lokey et al., 1991), ingesting sufficient amounts of calories post exercise and monitoring exercise duration as tolerated by individual women is advisable (Melzer, Schutz, Boulvain, et al., 2010).

1.16.2 Exercise intensity during pregnancy

Exercise guidelines define moderate intensity exercise as an activity that is performed with an energy requirement of three to five metabolic equivalents (METS; Artal & O’Toole, 2003). Activities such as cycling at 50-100 watts or walking at 4.8 – 5.5 km/h are considered moderate intensity for the general population (Ainsworth et al., 2011). In practice, the intensity of exercise for the pregnant women is more effectively monitored by either heart rate and ratings of RPE, or a combination of the two. The SOGC/CSEP guidelines suggest that for most pregnant women, exercise intensity
should range from 12-14 out of 20 on the Borg RPE Scale (Davies et al., 2003). In addition, target heart rate zones for moderate intensity exercise for a non-obese pregnant woman of 20-29 years of age is 135-150 bpm. This is lowered to 125-140 bpm for a woman of more than 40 years of age (Davies et al., 2003).

Although most guidelines promote moderate intensity exercise during pregnancy, there is limited research regarding exercise at higher intensities and accordingly, no evidence-based safe upper limit for the intensity of exercise has been established. Indeed, recently there has been increased interest in the amount of vigorous intensity exercise (~6-7 METS) pregnant women could engage in (Zavorsky & Longo, 2011b). Engaging in vigorous activity may be of particular relevance for the prevention of GDM based on a prospective study of pre-gravid physical activity and sedentary behaviours that reported an inverse association between vigorous activity and the risk of GDM (Zhang, Solomon, Manson, & Hu, 2006). However, the relationship between amount of vigorous intensity physical activity performed in pregnancy and the risk of developing GDM is not known.

Of importance, there is no evidence that acute bouts of exercise at a vigorous intensity is harmful for the mother and her developing fetus (MacPhail, Davies, Victory, & Wolfe, 2000; Marquez-Sterling et al., 2000; Szymanski & Satin, 2012; van Doorn, Lotgering, Struijk, Pool, & Wallenburg, 1992). For example, a study of the fetal heart rate response to a peak treadmill test in 45 women, divided into three equal groups of inactive, active and highly active women, found that overall fetal well-being (measured by fetal heart rate monitoring) was not compromised after short-duration, strenuous exercise (i.e. modified Balke protocol) (Szymanski & Satin, 2012). However, this study
did identify a sub-set of highly active women with evidence of transient fetal heart rate
decelerations and alterations in umbilical and uterine artery Dopplers immediately after
the test. Although a post-exercise biophysical profile performed using ultrasound
confirmed the wellbeing of fetus following vigorous exercise, these researchers
suggested that female athletes should be wary of pushing beyond a certain (high)
threshold of intensity (Szymanski & Satin, 2012). A separate study investigating
cardiovascular responses to cycling performed at an intensity of 75% $\dot{V}O_{2max}$ in 33
healthy women during pregnancy concluded that strenuous continuous exercise of
limited duration (approximately 15 min based on their results) was not harmful to the
mother or fetus (Doorn et al., 1992).

In addition to these studies examining a one-off bout of exercise, a program of regular
vigorous exercise performed three times a week has been reported to be safe for the
mother and her developing fetus (Marquez-Sterling et al., 2000). In this study,
participants were divided into an exercise group that performed a variety of exercise
activities for 15 weeks (three times per week) at heart rates of 150-156 bpm; and a
control group that did not exercise during the same time. Their results indicated that
both the exercise and control groups had no complications in any pregnancy outcome
measures, with all babies delivered healthy with no negative outcomes at term
(Marquez-Sterling et al., 2000). Subsequently, a prospective study ($n = 148$)
investigated whether vigorous exercise undertaken by recreational exercisers across
pregnancy was associated with reduced infant birth weight and gestational age at birth
(Duncombe et al., 2006). These researchers found that vigorous exercise was not
associated with significant reductions in mean birth weight and gestational age of the
infants (Duncombe et al., 2006).
Although vigorous activity may be safe and sustainable for physically conditioned pregnant women, the need for surveillance of fetal growth and maternal weight gain, as well as exercise duration and intensity is still imperative (Penney, 2008). Of relevance, it may be unwise to prescribe this type of exercise for previously sedentary pregnant women as the safety of vigorous intensity exercise for sedentary pregnant women remains to be established. Of relevance, interval-type training may be an alternative to continuous high intensity exercise to incorporate some vigorous exercise into the exercise routine of a pregnant woman. This form of exercise involves alternating periods of higher and lower intensity exercise over the exercise period, allowing for partial recovery, while still providing a higher intensity training stimulus.

Furthermore, there is evidence that interval training is better for glycemic control in patients with type 2 diabetes compared with traditional continuous moderate exercise (Tjonna et al., 2008). Specific to pregnancy, a 6-week program of stationary cycling including brief higher intensity intervals (consisting of 15–60 s at 75%–85% age-predicted $HR_{max}$ performed every 2 min, interspersed with lower intensity recovery between efforts) commenced at 28-29 weeks of pregnancy was recently conducted in women who were diagnosed with GDM (Halse et al., 2014). The intervention was well-tolerated, with excellent program compliance (96% of scheduled sessions completed) and was effective for improving daily postprandial glucose control, maternal fitness, and attitudes and intentions towards exercise, with no detrimental effects on obstetric outcomes (Halse et al., 2015; Halse et al., 2014). While the benefits of adding some vigorous intensity exercise to the exercise prescription in the form of interval training for glycaemic control and insulin resistance have been reported in a non-pregnant population, as well as pregnant women with GDM, the specific exercise prescription
required to prevent GDM remains to be determined. In addition, consideration must be
given to optimising the enjoyment of exercise for the pregnant woman. This has
important implications for exercise adherence (Ryan, Frederick, Lepes, Rubio, &
Sheldon, 1997). In particular, any potential benefits that may arise from performing
interval-type exercise would be meaningless if pregnant women did not enjoy this
format of exercise training. As such, future research investigating the effects of interval
training in pregnant women is warranted.

The optimal exercise intensity for GDM prevention is not known. One particular study
examined the effects of exercise intensity and duration on capillary glucose responses in
pregnant women at low and high risk of GDM (Ruchat et al., 2012). The study reported
that for women at risk of GDM, walking either at vigorous intensity (70% heart rate
reserve) for 25 min/session or at low intensity (30% heart rate reserve) for 35-40
min/session achieved the best decline in capillary glucose concentration. Interestingly,
engaging in more than 25 min of vigorous intensity exercise negated the decline in
capillary glucose concentration, at least acutely. Exercise intensity and duration did not
have a differential effect on the decreases in glucose concentrations in low risk women
(Ruchat et al., 2012). More research is needed to confirm the optimal exercise
prescription to prevent GDM.

1.16.3 Exercise mode during pregnancy

For women without contraindications to exercise, walking is a good form exercise for
previously sedentary pregnant women (Artal & O’Toole, 2003). Brisk walking provides
a full body workout and results in relatively low impact stress on the joints and muscles
(Wolfe, 2000; Davis et al., 2003). Walking is also a cost effective mode of exercise
which can be easily adopted by previously sedentary individuals. In addition, it is an exercise that the entire family can engage in together, negating potential issues of child care while a mother exercises. However, walking can sometimes be restricted by weather conditions (i.e. hot temperatures or wet weather unless a pregnant woman has access to an indoor treadmill), which may affect her adherence and consistency of exercise. Furthermore, as gestation advances, walking may become uncomfortable for some women due to alterations in the pelvic and hip joints (Ireland & Ott, 2000).

Swimming is another favourable mode of physical activity during pregnancy as it utilises large muscle groups (Artal & O’Toole, 2003; Davis et al., 2003) and has been shown to increase maternal fitness in previously sedentary women without compromising maternal and fetal wellbeing (Lynch et al., 2003). It also has added benefits such as reducing lower limb oedema and preventing overheating of the pregnant woman (Katz, McMurray, Berry, & Cefalo, 1988). In addition, the buoyancy provided by being in the water can provide relief for pregnant women suffering joint discomfort. However, unlike walking where a woman may be able to bring existing children, a woman might have to utilise child care services in order to go for a swim. Furthermore, the time and effort involved in getting to a swimming pool and the need for appropriate attire for the activity may become a barrier to exercise for some women (Evenson, Moos, Carrier, & Siega-Riz, 2009).

Stationary cycling is another recommended mode of exercise for pregnant women (Artal & O’Toole, 2003; Davis et al., 2003), and it may also potentially overcome some of the barriers to exercise associated with walking and swimming. Stationary cycling can be done indoors regardless of the weather and a woman can have her children in
close proximity while she exercises, potentially removing childcare constraints. The environmental temperature can be controlled with the use of a pedestal fan or an air-conditioning system. Lastly, an investigator can monitor the intensity of exercise training on a stationary bike with ease. Furthermore, there is evidence that women self-select to exercise at a higher intensity when stationary cycling compared with treadmill walking late in pregnancy (28-32 weeks of gestation) (Halse, Wallman, Newnham, & Guelfi, 2013). This is likely due to the weight-supported nature of stationary cycling, combined with the natural limit to the intensity of walking. Regardless, the resulting increase in energy expenditure for a given period of time appears to be beneficial for lowering postprandial glucose levels, with significantly lower 2-hr postprandial blood glucose levels following 30 min of self-paced stationary cycling compared with treadmill walking or a resting control (Halse, et al., 2013).

1.17 Are pregnant women exercising?

Despite the well documented benefits of a physically active lifestyle, an important issue is whether pregnant women are exercising enough, or if at all? In America, only approximately 40% of pregnant women exercise regularly, even though 92% are advised by their obstetricians to engage in 30 min of moderate activity on most days of the week (Field, 2012). Australian statistics indicate a similar trend, with less than 50% of pregnant women achieving recommended levels of exercise in pregnancy (de Jersey, Nicholson, Callaway, & Daniels, 2013). These low rates of physical activity during pregnancy appear to be attributed to the main barriers to exercise during pregnancy. These barriers include fatigue and discomfort as a result of pregnancy, concerns that exercise could be harming or depriving the fetus of energy for development (Melzer, Schutz, Soehnchen, et al., 2010; Poudevigne & O’Connor, 2006), as well as additional
fatigue arising from caring for existing children, household responsibilities and the lack of time associated with accomplishing the aforementioned maternal duties (Evenson et al., 2009; Marquez et al., 2009; Mottola & Campbell, 2003; Pereira et al., 2007). Demographic predictors such as low education and income have also been associated with low exercise levels in women of childbearing age (Gaston & Cramp, 2011; Gouveia et al., 2007). With statistics reporting a decreased likelihood of participation in leisure time physical activity in women with existing children, compared with women without children regardless of other factors (Brown, Mishra, Lee, & Bauman, 2000), there is an even greater challenge in encouraging exercise in pregnant women with children. As such, exercise interventions for pregnant women must be carefully designed with the aim of overcoming the many barriers to exercise listed above.

1.18 Overcoming barriers to exercise

Many of the barriers to exercise in pregnancy may be overcome by using a home-based, supervised training program, as opposed to centralised or institution-based program. Home-base exercise may remove barriers to exercise relating to a lack of transportation and potential issues relating to childcare. Of relevance, exercise adherence to a 12-month exercise program by overweight and obese (non-pregnant) women was shown to be enhanced by a home-based program, compared with an on-site program, as it negated the need to travel to sessions (Perri, Martin, Leermakers, Sears, & Notelovitz, 1997). Likewise, in a randomised controlled trial comparing the effects of hospital-based versus home-based exercise undertaken by cardiac patients, it was reported that home-based patients exercised an average of 6 sessions per week, while hospital-based patients reported only 3.7 sessions a week (Arthur, Smith, Kodis, & McKelvie, 2002).
These findings corroborate the effectiveness of home-based exercise as a tool to potentially encourage exercise participation in pregnant women.

1.18.1 Advantages of supervised home-based exercise for pregnant women

Specific to pregnancy, supervised, home-based exercise may overcome the need for childcare arrangements in order for a mother to attend a group session at an assigned institution, while the provision of a qualified exercise professional may assist with encouragement and motivation, as well as reassurance about the appropriateness and safety of exercise. In support of this notion, our pilot study which utilised supervised home-based exercise as an intervention for obese pregnant women resulted in 94% compliance rate over a 10 week period (Ong et al., 2009). Likewise, a 6-week supervised home-based exercise intervention for pregnant women diagnosed with GDM was recently reported to achieve 96% compliance rate (Halse, et al., 2014; Halse, et al., 2015).

Anecdotally, ensuring appropriate exercise intensity is achieved during home-based exercise may be compromised without the supervision of an investigator. In a study on the effects of a partially home-based exercise program for women with GDM (Avery, Leon, & Kopher, 1997), 33 women diagnosed with GDM at 28 weeks were randomly assigned to an exercise group (n = 15) or a no-exercise group (n = 14). Women in the exercise group either cycled under supervision (2 time per week) or walked/cycled independently (1-2 times per week), for 30 min at each session. Of note, participants of this study perceived their unsupervised home-based exercise as less intense than the supervised sessions. Importantly, with the supervision of an investigator, exercise
intensity can be monitored and recorded at each training session, avoiding the limitation associated with self-reporting of exercise intensity and frequency.

The presence of an exercise professional during home visitations may also reassure pregnant women about the safety of engaging in exercise. Moreover, in a one-on-one setting, the exercise professional could impart knowledge regarding exercise and provide tailored encouragement to the participant, thereby increasing their confidence and attitude towards exercise. Furthermore, women with children at home may also benefit from the social aspect of regular home visitations, which may indirectly contribute to the psychological wellbeing of the mother. A strategy of home-based supervised exercise is consistent with current trends in the health industry, in which care in the home is given priority wherever it may be cost effective and feasible.

1.19 Summary and statement of the problem
Over the past 25 years, there has been extensive research on the potential benefits and safety of exercise for the maternal-fetal unit, however, few studies to date have assessed the benefits of exercise for the prevention of GDM, and no studies have specifically focused on women with a history of the condition in a previous pregnancy. Potential limitations of the previous studies examining the effects of exercise on GDM include small sample sizes and inadequate adherence to the exercise prescribed. In addition, the population of women studied have primarily been healthy women, rather than those at elevated risk of GDM, which may limit the ability to detect significant differences between trials. To date, there has not been a large-scale randomised controlled trial that has examined the feasibility and effectiveness of a fully supervised, home-based
exercise program for preventing GDM in women with a history of the condition in a previous pregnancy.

1.20 Introductory research aims and hypotheses

Therefore, the main aim of this thesis was to conduct a randomised controlled trial examining the effect of a 14-week home-based, supervised exercise program commencing at 14 weeks of gestation on the recurrence of GDM. This thesis will also investigate the effects of the exercise intervention on other aspects of maternal and fetal wellbeing through measures of maternal fitness, weight gain and psychological wellbeing of the mother; as well as obstetric and neonatal outcomes. Before addressing this issue, a preliminary study aimed to establish the effect of adding brief higher intensity intervals to moderate-intensity continuous cycling on energy expenditure and the enjoyment of exercise in pregnancy as this information has important implications for exercise adherence and will inform the design of the 14 week exercise intervention.

It was hypothesised that a 14-week home-based, supervised exercise program would reduce the incidence of GDM in women with a history of the condition in a previous pregnancy. In addition, it was assumed that the exercise program would benefit pregnant women with a history of GDM through improved insulin sensitivity and glucose tolerance; aerobic fitness; body anthropometrics; mental health; blood lipid profile; and reduced rates of medical intervention during labour. It was also hypothesised that the exercise program will benefit the neonate through improved birth weight and neonate anthropometrics; lower rate of admission to neonatal special care units; and reduced incidence of neonate hypoglycaemia.
1.21 Organisation and structure of thesis

This thesis is organised into four chapters. Following Chapter 1 (Literature review) are two chapters based on an acute study investigating the effect of adding brief higher intensity intervals to continuous moderate intensity cycling on energy expenditure and enjoyment of exercise in late-gestation women (Chapter 2) and a randomised controlled trial investigating the effect of a 14-week supervised, home-based cycling program on the recurrence of GDM (Chapter 3). The final chapter (Chapter 4) integrates the findings of this thesis by providing an overall general discussion, including implications and directions for future research. All references are presented at the end of Chapter 4.
Chapter 2

The effect of adding brief higher intensity intervals to continuous moderate intensity cycling exercise on energy expenditure and enjoyment of exercise in pregnant women
This chapter is based on a manuscript prepared for publication in the BMC Pregnancy and Childbirth journal.
2.1 Abstract

Current guidelines recommend that pregnant women without contraindications should engage in 30 minutes or more of moderate intensity exercise on most days of the week, however, many women fail to achieve this goal. This study examined the effect of adding brief higher intensity intervals to traditional continuous moderate intensity exercise on energy expenditure and the enjoyment of exercise in late pregnancy. This is important to determine given that any additional energy expenditure resulting from higher intensity intervals may be meaningless if enjoyment is compromised, since long-term adherence will likely be low. In this study, 12 healthy pregnant women at 30 ± 1 weeks gestation, aged 35 ± 6 years with a BMI of 27.1 ± 4.3 kg/m\(^2\) performed either 30 minutes of continuous cycling exercise (CONT) at a steady power output equivalent to 65% age-predicted heart rate maximum or an equivalent period of interval cycling (INTV) consisting of continuous cycling at the same power output as CONT, but with the addition of six 15-s self-paced higher intensity efforts throughout, performed at regular intervals, on separate occasions in a counterbalanced order. Mean cycling power output, heart rate, oxygen consumption and energy expenditure were higher during INTV compared with CONT (\(P < 0.05\)). However, there was no difference in mean rate of perceived exertion between conditions. Enjoyment of exercise was higher with INTV (\(P = 0.01\)). The addition of six 15-s higher intensity intervals to continuous moderate intensity exercise effectively increased energy expenditure by 28%, at the same time as enhancing the enjoyment of exercise in late pregnancy. While these findings may be specific to recreationally active women, this study provides a rationale for future studies to examine the physiological and psychological responses to regular interval training during pregnancy to optimise exercise prescription.

Keywords gestation, exercise prescription, heart rate
2.2 Introduction

Stationary cycling is a recommended mode of exercise for pregnant women without obstetric complications (Artal & O'Toole, 2003) and may be preferable to walking during late gestation as it facilitates a higher self-paced intensity of exercise (Halse, Wallman, Newnham, & Guelfi, 2013). This in turn allows for greater energy expenditure and an augmented decline in postprandial glucose concentration for a given duration of exercise, without compromising the enjoyment of exercise (Halse et al., 2013). A program of regular home-based stationary cycling also appears to have favourable effects on maternal fitness and glucose tolerance in previously inactive obese pregnant women (Ong et al., 2009), and may assist with the management of daily postprandial blood glucose concentrations in women diagnosed with gestational diabetes mellitus (Halse, Wallman, Newnham, & Guelfi, 2014). However, the specific format and intensity of stationary cycling to safely optimise health and fitness benefits, together with enjoyment for the pregnant woman is not known.

Current guidelines recommend that pregnant women without medical and obstetric complications should engage in 30 minutes or more of moderate intensity exercise on most days of the week (Artal & O'Toole, 2003). However, with multiple barriers to exercise for busy mothers (Evenson, Moos, Carrier, & Siega-Riz, 2009), more than 50% of pregnant women do not achieve this (de Jersey, Nicholson, Callaway, & Daniels, 2013; Evenson & Wen, 2011). It has recently been suggested that vigorous intensity exercise may also be an important goal for some pregnant women (Kardel, Johansen, Voldner, Iversen, & Henriksen, 2009; Zavorsky & Longo, 2011a; Zavorsky & Longo, 2011b), but engaging in this level of exercise intensity may require more regular prenatal monitoring for maternal and fetal wellbeing (Penney, 2008). In addition,
vigorous intensity exercise may not be ideal for previously sedentary women. Incidentally, interval exercise is a popular way to incorporate some vigorous exercise into an exercise routine as it involves alternating periods of higher and lower intensity exercise over time. This allows for a higher intensity training stimulus with partial recovery between efforts. Indeed, in a non-pregnant population interval training has been reported to provide superior health benefits compared with moderate intensity continuous exercise (Helgerud et al., 2007; Little et al., 2011; Wisløff et al., 2007) and to enhance exercise enjoyment and adherence (Bartlett et al., 2011). The addition of brief higher intensity intervals to traditional continuous moderate intensity training may also provide an opportunity to safely optimise health and fitness benefits for the pregnant woman by increasing the energy expenditure of an exercise session, at the same time as maximising enjoyment. The latter is important given that the enjoyment of exercise is an important predictor of exercise adherence (Ryan, Frederick, Lepes, Rubio, & Sheldon, 1997). Meanwhile, strategies to increase overall energy expenditure during exercise may assist pregnant women to meet weekly volume-based targets with fewer exercise sessions or a reduced overall duration of exercise. Alternatively, increasing the overall weekly energy expenditure from exercise likely has benefits for the prevention of gestational diabetes, pre-eclampsia and excessive weight gain (Mudd, Owe, Mottola, & Pivarnik, 2013). In addition to these pregnancy-specific benefits, increasing energy expenditure through regular exercise has well-established benefits for reducing life-long all-cause mortality, risk of cardiovascular disease, type 2 diabetes and some cancers (Arem et al., 2015; Wen et al., 2011).

Previous research has shown that a 6-week program of stationary cycling including brief intervals (consisting of 15 to 60 seconds at 75%–85% age-predicted HR\textsubscript{max}}
performed every 2 minutes, interspersed with lower intensity recovery at 55%-65% age-predicted HR_{max} between efforts) commenced at 28-29 weeks of pregnancy is well-tolerated, with excellent program compliance (96% of scheduled sessions completed) (Halse, Wallman, Dimmock, Newnham, & Guelfi, 2015). Furthermore, this program was effective for improving daily postprandial glucose control, maternal fitness, and attitudes and intentions towards exercise, with no detrimental effects on obstetric outcomes (Halse et al., 2015). Whether similar health and fitness benefits may have been obtained with traditional moderate intensity exercise alone is not clear. Regardless, the first step towards addressing the issue of the optimal format and intensity of stationary cycling to safely optimise health and fitness benefits, together with enjoyment for the pregnant woman is to examine how the addition of brief self-paced higher intensity intervals to continuous exercise affects energy expenditure and the enjoyment of exercise in pregnancy. Understanding the acute responses to a single bout of exercise will provide justification for longer-term interventions of this nature in the future. Therefore, the aim of the present study was to investigate the effect of adding brief higher intensity intervals to traditional moderate-intensity continuous cycling on energy expenditure and the enjoyment of exercise in late pregnancy. Although higher intensity interval exercise that is performed for the same duration as continuous moderate-intensity exercise should result in greater energy expenditure, it is not known whether this would compromise exercise enjoyment in pregnancy. We hypothesise that the addition of brief higher intensity intervals to moderate intensity continuous cycling will increase the overall energy expenditure and intensity of exercise, at the same time as enhancing the enjoyment of exercise.
2.3 Methods

2.3.1 Participants

Healthy, non-smoking women \((N = 12)\) with uncomplicated singleton pregnancies were recruited upon entering their third trimester at 30 ± 1 weeks of gestation. Participants were 35 ± 6 years of age with pre-pregnancy body mass index (BMI) of 23.3 ± 3.0 kg/m² and BMI of 27.1 ± 4.3 kg/m² at the familiarisation session. Five of the participants were experiencing their first pregnancy, while the remaining seven already had ≥ one child. Pre-pregnancy exercise participation for all women was ≥ 1 session per week of at least 30 min of moderate intensity exercise. The PARmed-X for pregnancy (Wolfe & Mottola, 2002) was administered to ensure readiness to exercise. The study was approved by The University of Western Australia (UWA) Human Ethics Committee (Reference no. RA/4/1/6525) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

2.3.2 Study design

Participants attended a familiarisation session, followed by two experimental trials involving either continuous (CONT) or interval (INTV) stationary cycling performed on separate days in a counterbalanced Latin square design. The three visits were conducted within a 2-week period and were scheduled at least two days apart to minimise any effects from the previous session.

2.3.3 Experimental procedure

During the familiarisation session, body mass and height were measured. Aerobic fitness was assessed based on the heart rate responses to a modified version of the Aerobic Power Index test (Telford, Minikin, Hahn, & Hooper, 1989) on a stationary
cycle ergometer (Exertech Ex-10 front access cycle ergometer, Repco Cycle, Huntingdale, Victoria, Australia). This submaximal test has been previously applied in a pregnant population (Halse et al., 2015; Ong et al., 2009). Briefly, the modified test commenced with cycling at 25 W and increased by 25 W every two minutes until a heart rate equivalent to 75% of age-predicted maximum (HR\text{\text{max}} = 220 – age) was attained. The use of this sub-maximal exercise protocol based on age-predicted HR\text{\text{max}} was preferred over conducting a maximal exercise test to avoid subjecting the participants to the discomforts of maximal testing since they were recreational exercisers and did not engage in vigorous exercise in their current pregnancy.

Data from the aerobic test were used to determine the power output that would elicit 65% HR\text{\text{max}} for use in the subsequent experimental trials. Following this, participants cycled continuously at the prescribed power output for five to 10 minutes for the purpose of familiarisation. Next, participants performed two 15-second self-paced higher intensity efforts, with two minutes and 45 second of cycling at the power output equivalent to 65% HR\text{\text{max}} in between for recovery. The instruction given for these higher intensity efforts was to “increase the pedalling rate as much as you feel you comfortably can”. The duration of these intervals was based upon pilot work from our laboratory, along with a previous study that utilised higher intensity intervals in a 6-week exercise training intervention for women diagnosed with gestational diabetes (Halse et al., 2015; Halse et al., 2014), and an ongoing study by our laboratory implementing a 14 week interval training program during pregnancy.
2.3.4 Experimental trials

The subsequent two experimental trials were scheduled for the same time of day to control for circadian variation. At the first trial, participants were required to record all food and drink consumption and to replicate this for the subsequent trial. Quantity of sleep in the prior 24 h was also reported by each participant. Each participant then completed 30 minutes of cycling on the stationary cycle ergometer commencing and ending with a 5-minute warm up and cool down at 30 W. The 20-minute conditioning phase between the warm up and cool down consisted of the following performed in a counterbalanced order 1) continuous cycling (CONT) at a steady power output equivalent to 65% HR$_{\text{max}}$ or 2) interval cycling (INTV) consisting of continuous cycling at the same power output as CONT, but with the addition of six 15-second self-paced higher intensity efforts repeated every three minutes, performed with the same instructions as familiarisation. No minimum or maximum heart rate increase was applied during these self-paced efforts. The overall mean duration and intensity of exercise (65 to 75 %HR$_{\text{max}}$ and RPE 12-14) for both trials was consistent with recommendations for exercise in pregnancy (Artal & O'Toole, 2003; Davies, Wolfe, Mottola, & MacKinnon, 2003; RCOG, 2006), although it was expected that this threshold would be exceeded for brief periods in response to each self-paced interval.

2.3.5 Outcome measures

The heart rate response to exercise was monitored continuously throughout the entire trial and recorded at five minute intervals (Polar Heart Rate Monitor, Finland), along with the perceived level of exertion (RPE) using the 6 to 20 Borg Scale (Borg, 1982). In addition, RPE was recorded after each higher intensity interval and reassessed after one
minute of pedalling at the prescribed lower intensity. Mean power output (W) during
cycling was measured by a customised computer program interfaced with a stationary
cycle ergometer (Cyclemax; School of Sports Science, Exercise and Health, University
of Western Australia). In addition, expired air was collected between 20 to 25 minutes
of exercise using a computerised gas analysis system. This consisted of a ventilometer
(Universal ventilation meter, VacuMed, Ventura, California USA) that was calibrated
prior to each trial as per manufacturer specifications, using a one litre syringe and gas
analysers (Ametek Applied Electrochemistry S-3A/1 and CD-3A, AEI Technologies,
Pittsburgh, USA) that were calibrated using standard a reference gas of a known
physiological concentration. The measured oxygen consumption was used to calculate
the energy expenditure (McArdle, Katch, & Katch, 2010). A capillary blood sample (35
µL; Clinitube, Radiometer Medical, Denmark) was taken before and immediately after
each exercise trial and analysed for glucose concentrations (ABL™ 700 blood gas
system, Radiometer, Copenhagen, Denmark).

The enjoyment of exercise was assessed using the Physical Activity Enjoyment Scale
(PACES) (Kendzierski & DeCarlo, 1991) immediately following each trial. Briefly, this
required participants to rate "how you feel at the moment about the physical activity you
have just done" using 18 statements on a 7-point bipolar scale (e.g. “I enjoyed it - I
hated it”, “It was very unpleasant - It was very pleasant”). Eleven of 18 items were
reverse scored. After reverse scoring items as appropriate, each item was summed to
give a total score out of 126, with a higher PACES score reflecting greater levels of
enjoyment. In addition, participants provided written responses to the questions “Did
you prefer the continuous cycling session or the interval cycling session?” and “why?”
based on the two trials that they had performed. Next, they were asked which format of
exercise they would like to perform if they were to engage in a 3-month cycling program in pregnancy and were asked to justify their choice.

2.3.6 Statistical analysis

Heart rate, cycling power output, energy expenditure, oxygen consumption, RPE and PACES (enjoyment) were compared between trials using one-way repeated measures analysis of variance (ANOVA). The blood glucose response to exercise was compared using two-way (time x condition) repeated measure ANOVA. Statistical significance was accepted as a $P$ value of $\leq 0.05$ (SPSS 20.0 for windows computer software package).

2.4 Results

Sleep duration the night prior was well-matched between trials ($P = 0.26$), with a mean of $7.5 \pm 1.2$ hours of sleep before the CONT trial and $7.3 \pm 1.0$ hours before the INTV trial. Similarly, mean resting heart rate was $89 \pm 10$ bpm before the CONT and $92 \pm 13$ bpm before INTV ($P = 0.29$). The characteristics of the exercise trials are displayed in Table 1. Mean power output, heart rate, oxygen consumption and energy expenditure were higher during the 20-minute conditioning phase of INTV compared with CONT (Table 1, $P < 0.05$). Of note, the maximum HR reached during the brief self-paced higher intensity intervals was $154 \pm 12$ bpm [$83 \pm 6$ % age-predicted $HR_{\text{max}}$]. Mean blood glucose concentration was similar prior to the start of both trials and decreased in response to exercise ($P < 0.05$), with no difference between conditions.

Despite the higher overall intensity of INTV compared with CONT, there was no significant difference in mean RPE between conditions. Enjoyment of exercise (PACES
score) was higher in INTV compared with CONT ($P = 0.01$; Table 1). From the written responses provided by the participants, all 12 stated that they preferred INTV over CONT. Reasons included that it was more “interesting”, “challenging”, provided a “better workout” and made time “go faster” because the exercise was “broken up”. One participant stated that she had “expected to prefer the continuous cycling” but found that INTV gave her a “sense of accomplishment and better understanding of her exercise capacity”. However, when asked which type of exercise women would prefer if it was a 3-month, thrice weekly cycling program, one participant preferred CONT, eight participants preferred INTV and three preferred a mixture of CONT and INTV.
Table 2.1. Physiological and psychological responses to continuous moderate intensity cycling (CONT) compared with an equivalent duration of interval cycling (INTV) involving the addition of six 15-s self-paced higher intensity efforts (n = 12); mean ± SD.

<table>
<thead>
<tr>
<th>Physiological measures during 20-min conditioning</th>
<th>CONT</th>
<th>INT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean power output (W)</td>
<td>78 ± 22</td>
<td>99 ± 18&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean power output&lt;sub&gt;15 sec effort&lt;/sub&gt; (W)</td>
<td>NA</td>
<td>281 ± 72</td>
</tr>
<tr>
<td>Mean heart rate (bpm)</td>
<td>126 ± 8</td>
<td>136 ± 11&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean % HR&lt;sub&gt;max&lt;/sub&gt;</td>
<td>68 ± 4</td>
<td>73 ± 5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>V&lt;sub&gt;O&lt;/sub&gt;&lt;sub&gt;2&lt;/sub&gt; (L.min&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>1.23 ± 0.24</td>
<td>1.57 ± 0.28&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Est. energy expenditure (kJ)</td>
<td>506 ± 99</td>
<td>645 ± 116&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Glucose&lt;sub&gt;pre&lt;/sub&gt; (mmol&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>5.9 ± 1.0</td>
<td>5.6 ± 1.2</td>
</tr>
<tr>
<td>Glucose&lt;sub&gt;post&lt;/sub&gt; (mmol&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>4.8 ± 0.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.6 ± 0.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Psychological measures during 20-min conditioning</th>
<th>CONT</th>
<th>INT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RPE&lt;sub&gt;overall&lt;/sub&gt;</td>
<td>11 ± 2</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>Mean RPE&lt;sub&gt;15s_effort&lt;/sub&gt;</td>
<td>NA</td>
<td>16 ± 1</td>
</tr>
<tr>
<td>Enjoyment (PACES score)</td>
<td>82 ± 21</td>
<td>101 ± 12&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> denotes significant difference between conditions (P < 0.05)
<sup>b</sup> denotes significant difference pre/post within condition (P < 0.05)

Note: % HR<sub>max</sub>, percentage age-predicted heart rate maximum; RPE, rate of perceived exertion from of 6–20 scale; 6 = no exertion, 20 = maximal exertion; Higher PACES score indicate greater enjoyment of exercise.
2.5 Discussion

This study compared the effect of adding brief self-paced higher-intensity intervals to continuous moderate intensity stationary cycling on enjoyment and the physiological responses to exercise in the third trimester of pregnancy. Although interval training of this nature has recently been utilised in women diagnosed with gestational diabetes with favourable effects on maternal fitness and postprandial glucose control, no previous studies have compared the effects of continuous and interval exercise in pregnancy. The addition of six 15-second higher intensity intervals (90 second in total) to 20 minute of continuous moderate intensity cycling significantly increased the energy expenditure by 28%. Importantly, the increased overall exercise intensity with INTV was not associated with a marked difference in RPE. Overall, the session of continuous cycling was perceived as “fairly light” (rating of 11) while the session involving additional brief intervals was perceived as between “fairly light” and “somewhat hard” (rating of 12). This overall RPE rating of INTV indicated a moderate intensity exercise session despite the brief intervals themselves being rated ‘hard’. In addition, exercise enjoyment was higher for INTV compared with CONT, and INTV was the preferred mode of exercise compared with CONT. These findings from a single session of exercise provide a rationale to further examine the effect of incorporating brief self-paced intervals into exercise training for pregnant women which in turn may have implications for exercise prescription.

The greater physiological responses (i.e. heart rate, oxygen consumption and energy expenditure) associated with INTV were expected given that the protocols were not designed to match total work output. The alternative study design of matching total work between CONT and INTV would have required a greater duration of exercise for
CONT. Given that a “lack of time” is one of the main barriers to exercise in pregnancy (Evenson et al., 2009), our preference was to match for exercise duration and examine the addition of brief intervals to CONT since the possibility of achieving greater exercise stimulus and energy expenditure within an equivalent amount of time is likely appealing to pregnant women. Of particular interest, the higher overall intensity of INTV was not associated with increased overall perception of effort. This was despite the brief intervals themselves being rated as ‘hard’ in isolation. The overall ‘moderate’ perception of effort with INTV is likely related to the provision of sufficient active recovery at a lower intensity between efforts – an important consideration for ensuring an appropriate overall intensity for the pregnant woman. Furthermore, despite the addition of these brief intervals, INTV was associated with higher ratings of enjoyment based on the PACES. This is consistent with other studies by us and others that have reported higher intensity interval exercise to be more enjoyable than traditional continuous exercise in non-pregnant populations (Bartlett et al., 2011; Crisp, Fournier, Licari, Braham, & Guelfi, 2012). In the present study, the pregnant women reported INTV as more “interesting” and “challenging” compared with CONT. Since enjoyment of exercise is a major predictor of attendance and adherence to exercise (Ryan et al., 1997), the greater enjoyment associated with INTV may have implications for exercise prescription during pregnancy to promote regular exercise participation. Indeed, when asked which type of exercise women would prefer if it was a 3-month, thrice weekly cycling program, the incorporation of INTV was strongly supported. However, future research is needed to confirm if the findings from a single isolated session of exercise will transfer to regular participation. In addition, it is important to note that enjoyment should not override safety, and so utilisation of this form of exercise training in future studies should include monitoring of maternal and fetal outcomes. Although the fetal
responses to the exercise trials were not monitored here, the perceived exertion and heart rate response to the intervals in the present study were consistent with that reported by Halse and colleagues (Halse et al., 2015) who observed no detrimental effect on obstetric and neonatal outcomes following 6 weeks of interval exercise training commenced upon diagnosis of gestational diabetes. Furthermore, the addition of six 15-second higher intensity intervals (90 seconds in total) is of much lesser duration than that maintained by pregnant women during maximal exercise testing (Lotgering, van Doorn, Struijk, Pool, & Wallenburg, 1991; MacPhail, Davies, Victory, & Wolfe, 2000; Sady et al., 1988). However, confirmation of the safety of this mode of exercise training will be needed for programs of longer duration commenced earlier in pregnancy.

A limitation of the current study is the specific focus on healthy women in the third trimester of pregnancy. Thus the findings cannot be generalized to all pregnant women. In addition, the participants included in the present study were recreationally active. It is possible that previously sedentary women may respond differently. With respect to the addition of brief intervals to a regular training program, it is also possible that responses may vary as pregnancy progresses, given the variability in a woman’s emotional and physiological state. Accordingly, this format of exercise needs to be tested on a larger sample of pregnant women of varying exercise habits. In particular, the safety of the women and her fetus must be monitored closely if this format of exercise is performed by previously sedentary women. Nevertheless, this acute study provides the basis for future studies to examine the effects of regular INTV exercise training during pregnancy on maternal and foetal health and wellbeing. Given the many health benefits of regular exercise during pregnancy (Artal & O'Toole, 2003; Zavorsky & Longo, 2011a,b),
whether the greater exercise stimulus associated with interval exercise training can benefit the prevention and/or management of certain pregnancy complications such as gestational diabetes also remains to be determined. In the present study, blood glucose concentrations were acutely reduced to a similar extent by both exercise protocols, but since blood glucose was not elevated to start with, future studies in women with impaired glucose tolerance may be warranted.

**Conclusion**

In conclusion, the purpose of our study was to investigate the effect of adding brief higher intensity intervals to moderate-intensity continuous cycling on energy expenditure and the enjoyment of exercise in late pregnancy. We have shown that interval cycling, consisting of brief periods of elevated intensity and sufficient recovery at moderate intensity is well tolerated and rated as more enjoyable by women in the third trimester of pregnancy compared with traditional continuous moderate intensity cycling. These findings from a single session of exercise provide a rationale to further examine the effect of incorporating brief self-paced intervals into exercise training for the pregnant woman. However, future research is needed to support the safety and effectiveness of regular performance of this type of training during pregnancy to allow for evidence-based guidelines to inform exercise prescription for the pregnant woman to optimise physiological outcomes as well as enjoyment and long-term adherence to exercise.
Chapter 3

The Cycle Study: A randomised controlled trial of cycling to prevent the recurrence of gestational diabetes mellitus
This chapter is based on a randomised controlled trial conducted to assess the effectiveness of a supervised home-based exercise program for the prevention of GDM in women with a history of the condition.
3.1 Abstract

Gestational diabetes (GDM) can have serious health consequences for both the pregnant woman and her child. These include antenatal complications such as pre-eclampsia and macrosomia, as well as an elevated risk of developing type 2 diabetes later in life. For women with a history of GDM, the risk of recurrence may be as high as 69%. This randomised controlled trial investigated the effect of a supervised home-based program of stationary cycling on the recurrence and severity of GDM, together with other aspects of maternal health, obstetric and neonatal outcomes. Non-diabetic women with a history of GDM in a previous pregnancy were randomised to an exercise intervention (EX; n = 85) or to a control group (CON; n = 87) at 13 ± 1 weeks of pregnancy. The exercise intervention involved a 14 week supervised, home-based stationary cycling program, performed three times per week for 30-60 min. GDM diagnosis was based on a post-intervention 75 g OGTT. Other outcome measures including maternal fitness and psychological wellbeing were assessed pre- and post-intervention. The recurrence rate of GDM was similar between groups (CON 40%; EX 41%; \( P = 0.95 \)). Likewise, the severity of GDM at diagnosis was unaffected by the exercise program, with similar glucose and insulin responses to the OGTT. Maternal fitness was improved by the exercise program (\( P < 0.01 \)), as were some markers of psychological well-being (i.e. lowered negative emotional symptoms; \( P = 0.02 \)). There were no differences in obstetric and neonatal outcomes between groups (\( P > 0.05 \)). Regular supervised home-based exercise commenced at 14 weeks of pregnancy benefits maternal fitness and psychological well-being, but does not prevent the recurrence of GDM. These results may highlight the need for a life-course approach to the prevention of chronic diseases.
3.2 Introduction

Gestational diabetes mellitus (GDM) affects up to 28% of pregnancies worldwide (Jiwani et al., 2012) and the incidence is rising (Ferrara, 2007). This state of carbohydrate intolerance with onset or first recognition during pregnancy (Bottalico, 2007) puts women at increased risk of many acute pregnancy complications such as pre-eclampsia, infection and postpartum haemorrhage (Dempsey et al., 2005); as well as an increased risk of developing type 2 diabetes and metabolic syndrome in later life (Lauenborg, Mathiesen, & Damm, 2005). For the fetus, an elevated maternal glucose concentration promotes excessive growth and increased birth weight (macrosomia) (Persson, Eriksson, & Hanson, 2005), which may result in increased incidence of shoulder dystocia, birth injury, surgical intervention and increased rates of admission to a neonatal care unit (Andreasen et al., 2004). Later in life, these offspring have an increased prevalence of obesity, type 2 diabetes and metabolic syndrome (Boney et al., 2005). Risk factors for GDM include increased maternal age, obesity and physical inactivity, and since these risk factors tend to worsen in subsequent pregnancies, the recurrence rate of GDM is estimated be as high as 69% (Ben-Haroush et al., 2004).

There is some evidence to suggest that exercise may offer a potential strategy to prevent GDM. Epidemiological data indicate that being physically active before and during pregnancy is associated with a reduced rate of glucose intolerance and GDM (Dempsey et al., 2005; Dempsey, Sorensen, et al., 2004; Oken et al., 2006; Zhang et al., 2006). In addition, experimental studies have shown that regular exercise during pregnancy may attenuate the typical physiological decline in glucose tolerance that occurs in pregnancy (Barakat, Cordero, Coteron, Luaces, & Montejo, 2012; Ong et al., 2009). However, there are few randomised controlled trials investigating the effect of regular exercise for
the prevention of GDM with conflicting outcomes (Barakat et al., 2013; Cordero et al., 2014; Stafne et al., 2012) and no trials have focused on women with a history of the condition who are at the highest risk. Furthermore, compliance to prescribed exercise interventions has been reported as a limiting factor in some trials (Stafne et al., 2012). The issue of enhancing exercise compliance in pregnancy is important given that fewer than half the number of women who are pregnant engage in regular exercise (de Jersey et al., 2013; Evenson & Wen, 2010; Field, 2012). Common barriers to exercise in this population include a lack of time associated with managing a household and caring for existing children, tiredness, physical limitations and concerns about safety (Evenson & Bradley, 2010; Marquez et al., 2009; Mottola & Campbell, 2003; Pereira et al., 2007). Supervised, home-based exercise training may overcome many of these barriers to regular maternal exercise. In support of this notion, we have previously demonstrated exceptional compliance to a home-based supervised exercise program in obese pregnant women (94%) (Ong et al., 2009) and women diagnosed with GDM (96%) (Halse et al., 2015). Accordingly, the aim of this study was to investigate the effect of a 14-week supervised, home-based exercise program commenced at 14 weeks of pregnancy on the recurrence and severity of GDM in women with a history of the condition in a previous pregnancy. The effect of the intervention on maternal cardiovascular fitness, body anthropometrics, psychological well-being and obstetric outcomes were also examined.

3.3 Methods

3.3.1 Participants

Pregnant, non-diabetic women with a history of GDM in a previous pregnancy were recruited through public antenatal clinics, private obstetricians, general practitioners and ultrasound practices around the Perth metropolitan area from June 2011 to July 2014.
Participants were eligible for inclusion in the study if they were less than 14 weeks pregnant, over 18 years of age, able to participate in a supervised 14-week home-based exercise program and able to understand the implications of participation in the study. Women with pre-existing diabetes (type 1 or 2), cardiac disease, multiple pregnancy or a medical condition that restricted exercise participation, or those who were already engaged in a structured exercise program at the time of recruitment were not eligible for the study. The study was approved by the King Edward Memorial Hospital Ethics Committee and The University of Western Australia Human Ethics Committee. All participants provided informed written consent at the initial assessment and were advised that they could withdraw from the study at any time during the intervention.

3.3.2 Experimental design

This single-centred randomised controlled trial was registered at www.clinicaltrials.gov (identifier: NCT01283854) and conducted in accordance with the CONSORT Statement (Moher, Schulz, & Altman, 2001). Eligible participants were randomised between 12 – 14 weeks of pregnancy to either an exercise intervention group (EX) or a control group (CON) using a custom-designed computer program which stratified by body mass index (BMI < 30; 30-34.9 or > 35 kg/m²) and maternal age (< 35 y or ≥ 35 y). Each participant entered the stratification factors into the program and was informed of her allocation on the next screen of the computer program. Outcome measures were assessed pre- and post-intervention as detailed below.

3.3.3 Exercise intervention

Participants randomised to EX engaged in a 14-week, thrice weekly stationary cycling program that commenced seven days after randomisation. A stationary, upright cycle
ergometer (Maxx Kh-805 Programmable Upright bike; Nordic Fitness) was delivered to each participant’s home for her use during the intervention (Figure 3.1). All sessions were home-based and fully supervised by an exercise physiologist from the School of Sport Science, Exercise and Health, UWA (either the PhD candidate or one of several research assistants) (Figure 3.2). The exercise physiologist would travel to the home of each participant thrice weekly to prescribe and monitor the duration and intensity of cycling performed. All exercise physiologists underwent a formal induction program with the PhD candidate to ensure that all exercise prescription was standardised amongst the participants in EX (see Appendix D for Induction Protocol).

At each session, participants’ readiness for exercise was confirmed by measuring blood pressure and verbally assessing wellbeing. Exercise sessions were postponed if resting blood pressure was > 140/90 mmHg, or if a participant was unwell or experiencing vaginal bleeding/spotting. Regarding the latter, the participant was referred to her antenatal carer to be cleared for exercise before she resumed the exercise program.
Figure 3.1. The delivery of an upright cycle ergometer to a participant’s home for the duration of the intervention.
NOTE: Figure 3.2 removed due to confidentiality requirements of participants.

Figure 3.2. A home-based exercise session on the upright stationary cycle ergometer, supervised by a research assistant.
Exercise training was performed in accordance with the American College of Obstetricians and Gynecologists (ACOG) exercise guidelines for pregnant women (Artal & O'Toole, 2003) and the Canadian guidelines for exercising during pregnancy (Davis et al., 2003). Each session commenced with a 5-min warm-up consisting of pedalling at an intensity of 55%–65% age-predicted heart rate maximum ($HR_{\text{max}} = 220$-age) and rate of perceived exertion (RPE) of 9-11 on the 6-20 Borg scale (Borg, 1982). The subsequent conditioning period was broken up into different phases. These phases included alternating 5-min periods of a) continuous moderate-intensity cycling (65%–75% $HR_{\text{max}}$; target RPE 12–13) and b) intervals of varying intensity consisting of 15–30 s of higher-intensity bouts (75%–85% $HR_{\text{max}}$; target RPE 14–16) repeated every 2 min, interspersed with lower intensity cycling between efforts (65%–75% $HR_{\text{max}}$; RPE 12-13). These higher intensity bouts were achieved by either an increase in pedalling rate (15-s intervals) or cycling resistance (30-s intervals). This combination of continuous moderate intensity cycling and higher intensity interval cycling was based on our previous work showing that adding brief higher intensity intervals to moderate intensity continuous cycling enhances energy expenditure and exercise enjoyment in pregnant women (Chapter Two). The cycling resistance was adjusted as appropriate to maintain the required intensity for each phase of the session. A 5-min cool-down of stationary cycling concluded each session (55%–65% $HR_{\text{max}}$; target RPE 9-11), followed by light static stretching of each main muscle group. The duration of each exercise session was progressively increased by 5 min increments every two to three weeks as tolerated over the 14-week intervention from 20-30 min to a maximum session duration of 60 min. The degree of progression was dependant on the baseline fitness level of the woman, as well the incidence of pregnancy symptoms (i.e. fatigue, morning sickness, a bad night’s sleep) throughout the 14 week period (see Appendix D for sample program).
3.3.4 Control group

Women randomised to CON received routine, regular antenatal care.

3.3.5 Assessment of outcome measures

Participants visited our laboratory at the School of Sport Science, Exercise and Health at UWA for the assessment of a number of outcome measures (i.e. maternal cardiovascular fitness, body anthropometric measurements, and psychological wellbeing) at 12 – 14 weeks gestation (pre-intervention) and again at 28 - 29 weeks of pregnancy (post-intervention). In addition, each participant was required to visit a local community pathology centre (PathWest) on a separate occasion (both pre- and post-intervention) where blood was sampled in the fasted state and in response to a 75 g oral glucose tolerance test (OGTT; at 30, 60, 90 and 120 min post-ingestion). For all assessments, participants were required to avoid any moderate-vigorous physical activity in the preceding 48 hours, and all blood testing was performed in an overnight fasted state (no food or drink except for water from 2200 h the night before).

3.3.5.a Assessment of GDM incidence

Diagnosis of GDM was based on a fasting venous blood glucose ≥ 5.5 mmol/L and/or a 2-h OGTT venous glucose ≥ 8.0 mmol/L (Martin, Vogue, Dargaville, Ericksen, & Oats, 1991). These diagnostic criteria are the most widely adopted in Western Australia despite the revised recommendations from Australasian Diabetes in Pregnancy Society (ADIPS) in 2012 (fasting blood glucose > 5.1 mmol/L; 1-hour blood glucose level > 10.0 mmol/L; and/or 2-hour blood glucose level > 8.1 mmol/L) (Nankervis et al., 2012).
3.3.5.b Assessment of glucose tolerance and insulin sensitivity

Fasting glucose and insulin concentrations, together with glucose tolerance and insulin sensitivity were determined from the 75 g OGTT. More specifically, fasting glucose and insulin values were used to assess insulin sensitivity using the homeostatic model of assessment (HOMA-IR) calculated by the following equation as first described by Matthews et al. (1985) which correlates strongly ($R_s = 0.88$, $P < 0.0001$) with the euglycaemic clamp method (DeFronzo, Tobin, & Andres, 1979):

$$HOMA-IR = \frac{\text{Fasting Glucose} \times \text{Fasting Insulin}}{22.5}$$

For the glucose and insulin responses to the 75 g glucose load, area under the curve was calculated using the trapezoidal rule by computing the area of trapezoids defined by the five time points from fasting to 120 min after OGTT. Additionally, the insulin sensitivity index (ISI)(Matsuda & DeFronzo, 1999) was calculated from the glucose and insulin responses to the OGTT using the following formula:

$$\frac{10000}{\sqrt{(\text{FPG} \times \text{FPI}) \times (\bar{G} \times \bar{I})}}$$

where 10000 represents a constant that computes numbers ranging from 0 to 12, FPG is fasting plasma glucose (mg/dl), FPI is fasting plasms insulin ($\mu$U/ml), $\bar{G}$ is mean OGTT glucose concentration and $\bar{I}$ is mean OGTT insulin concentration. This method correlates strongly ($r^2 = 0.64$) with the gold-standard euglycemic insulin clamp method (Kirwan, Huston-Presley, Kalhan, & Catalano, 2001).

Finally, glycosylated haemoglobin (HbA1c) and serum c-peptide were assessed from the fasting venous blood sample to provide a mean blood glucose profile three months prior and an indication of insulin production over time respectively.
3.3.5.c Assessment of cardiovascular health and fitness

Cardiovascular health was assessed via resting heart rate, blood pressure and measurements of fasting cholesterol and triglyceride. In addition, cardiovascular fitness was assessed based on heart rate and oxygen consumption ($\dot{V}O_2$) responses to the Aerobic Power Index test (Telford et al., 1989) on a stationary cycle ergometer (Exertech Ex-10 front access cycle ergometer, Repco Cycle, Huntingdale, Victoria, Australia). This test has been previously applied in a pregnant population (Halse et al., 2015; Ong et al., 2009). Briefly, this test commenced with cycling at 25 W and increased by 25 W every min until a heart rate equivalent to 75% of age-predicted maximum (HR$_\text{max}$) was attained. In addition, participants breathed through a mouthpiece (Hans Rudolph Inc, Kansas, USA) connected to a computerised gas analysis system (Universal ventilation meter, VacuMed, Ventura, California USA; Ametek Applied Electrochemistry S-3A/1 and CD-3A, AEI Technologies, Pittsburgh, USA) to measure $\dot{V}O_2$ for the duration of the cycling test. Fitness was expressed as both power output (W) and the $\dot{V}O_2$ (L/min) at 75% HR$_\text{max}$.

3.3.5.d Assessment of maternal body anthropometrics

Height, body mass, five peripheral skinfolds (biceps, triceps, subscapular, mid-thigh and calf) and four limb girths (upper relaxed arm, upper flexed arm, thigh and calf) were assessed. Skinfolds and girths of the mid torso were excluded due to pregnancy.

3.3.5.e Assessment of psychological wellbeing

Psychological well-being was assessed pre- and post-intervention using the 21-item version of the Depression Anxiety Stress Scale (DASS$_{21}$) (Henry & Crawford, 2005) which possesses good internal consistency and has been validated as a measure of
general psychological distress (Osman et al., 2012). In addition, the Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, & Sagovsky, 1987) was administered given its routine instrument use both antenatally and postnatally in our clinical setting. A modified, nine-item version of the Social Physique Anxiety Scale (SPAS) (Hart, Leary, & Rejeski, 1989; Motl & Conroy, 2000) was administered to monitor concerns about negative evaluations from others due to the physical changes associated with pregnancy.

3.3.5.f Assessment of habitual dietary intake and physical activity behaviour

Each participant completed a 7-day food diary before and after the intervention to monitor dietary habits over the intervention period. Participants were asked to provide as much detail as possible of the foods and drinks consumed over a seven day period, including the quantities and brands. Participants were instructed to directly measure their intake as much as possible (i.e. using measuring cups, or weighing scales). Mean daily nutritional intake (total energy, carbohydrate, fat, protein, sugar and fibre) was determined using a commercially available program (Foodworks, Xyris Software, Highgate Hill, Queensland, Australia).

Similarly, physical activity was monitored for a 7-day period pre- and post-intervention using an accelerometer (ActiGraph, Pensacola, FL, USA) worn on the right hip at the site of the anterior superior iliac spine. The total numbers of steps, estimated energy expenditure, time sedentary and time in light and moderate intensity physical activity per day were determined using the ActiLife software (version 6.9.3, 2014). Changes in exercise habit strength resulting from participation in the exercise program were assessed by administering the moderate-to-vigorous physical activity (MVPA) Habit Strength Questionnaire before and after the intervention (Grove, Zillich, & Medic,
This instrument provides scores for four conceptually-distinct components of exercise habits (patterning of action, automaticity, stimulus-response bonds, and negative consequences for non performance).

3.3.5.g Assessment of obstetric and neonate outcomes

Relevant obstetric and neonatal outcomes were extracted from hospital records by research midwives from the School of Women’s and Infants’ Health at UWA following delivery. Obstetric outcomes included rates of onset of labour, mode of delivery and obstetric complications. Neonatal outcomes included rates of preterm birth, gestational age at birth and rates of neonate complications and admission to special care nursery. Birth weight was used to calculate birth weight percentiles to determine size of neonate for gestational age (i.e. large or small for gestational age).

3.3.5.h Statistical analysis

The primary outcome of the study was GDM in the current pregnancy. Data from King Edward Memorial Hospital (Perth, Western Australia) indicated that in our population of pregnant women with a previous history of GDM, the overall risk of recurrence was 55%, a figure consistent with the published literature (Bottalico, 2007; Pivarnik et al., 2006). A sample size of 180 (90 women in each group) was required to attain 80% power to detect a 40% reduction in the incidence of GDM, from 55% to 33%, when performing a test of proportions at 5% significance level.

Continuous data was summarised using means and standard deviation or medians and interquartile ranges, depending on data normality. Categorical data was summarised using frequency distributions. The incidence of GDM was compared using Chi-square
test. The glucose and insulin responses to the OGTT were compared between groups pre- to post-intervention using three-way (group x pre-post x time) repeated measures analysis of variance. Insulin sensitivity, maternal fitness, body anthropometrics, psychological wellbeing, physical activity levels and daily nutritional intake were compared between groups pre- to post-intervention using two-way (group x time) repeated measures analysis of variance. Statistical analysis was conducted based on intention-to-treat. All hypothesis tests were two-sided and conducted at a 5% significance level. Data analysis was conducted using SPSS statistical software (SPSS 20.0 for windows).

### 3.4 Results

The CONSORT flow chart is displayed in Figure 3.3. In all, 318 women were assessed for eligibility for the study and 205 provided written consent to participate in the trial and completed baseline pre-intervention assessments at 13 ± 1 week of gestation. Of these 205 women, 33 were excluded from the trial after baseline assessment due to an elevated pre-intervention OGTT leaving 172 randomised to EX (n = 85) and CON (n = 87). The baseline characteristics of these women are shown in Table 3.3. Pre-pregnancy BMI was not recorded as participants were unable to accurately recall their pre-pregnancy body mass at the time of baseline testing. Two women experienced miscarriages at 19 weeks gestation and one experienced a pregnancy loss at 21 weeks gestation before the assessment of outcome measures (CON = 2; EX = 1). All remaining women completed the post-intervention OGTT (28 ± 1 week gestation), however, twelve women (CON = 9; EX = 3) failed to complete the additional post-intervention assessments of fitness, body anthropometrics and psychological well-being.
3.4.1 Supervised home-based exercise intervention

Mean compliance to the supervised, home based exercise intervention was 83%, with a mean of seven sessions missed out of a total possible 42 sessions (3 sessions for 14 weeks). The mean heart rate during the conditioning phase was 130 ± 10 bpm (70 ± 5% age-predicted HR\textsubscript{max}). Participants reported a mean session RPE of 13 ± 1 indicating that exercise intensity was perceived to be “somewhat hard”. Of note, exercise duration increased from a mean of 28 ± 4 min in the first week to 47 ± 11 min in the last week of the intervention. Of note, the total distance travelled to deliver the exercise intervention to the participants was approximately 137,000 km over a three year period (Figure 3.4).
Figure 3.3. CONSORT flow chart for The Cycle Study (2011-2014)

Assessed for eligibility (n = 318)

Excluded (n = 113)
  a. Not meeting inclusion criteria (n = 76)
  b. Declined to participate (n = 37)

Randomised (n = 205)

Excluded (n = 33)
  - Elevated OGTT at baseline

Control Group (CON)
  Allocated to standard care (n = 87)
  Discontinued standard care
    - Miscarriage (n = 2)
  Analysed for primary outcome (n = 85)
  Analysed for secondary outcomes (n = 76)
    - Did not attend post-intervention assessment (n = 9)

Allocation

Exercise Group (EX)
  Allocated to intervention (n = 85)
  Discontinued intervention
    - Pregnancy loss (n = 1)
  Analysed for primary outcome (n = 84)
  Analysed for secondary outcomes (n = 81)
    - Did not attend post-intervention assessment (n = 3)
Table 3.1. Baseline characteristics of women randomised to a 14-week supervised home-based exercise intervention (EX) or standard care (CON) [(mean ± SD)/n (%)/median (interquartile range)].

<table>
<thead>
<tr>
<th>Variable</th>
<th>CON (n = 87)</th>
<th>EX (n = 85)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (y)</td>
<td>33.8 ± 3.9</td>
<td>33.6 ± 4.1</td>
<td>0.750</td>
</tr>
<tr>
<td>Highest SEAIFA IRSD quintile*</td>
<td>49 (56.3)</td>
<td>49 (57.6)</td>
<td>0.768</td>
</tr>
<tr>
<td>Ethnicity**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>68 (78)</td>
<td>76 (89)</td>
<td>0.071</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>-</td>
<td>4 (5)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (5)</td>
<td>6 (7)</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparous</td>
<td>71 (82)</td>
<td>58 (68)</td>
<td>0.077</td>
</tr>
<tr>
<td>Multiparous</td>
<td>16 (18)</td>
<td>27 (32)</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 24.9 kg/m²</td>
<td>48 (55)</td>
<td>37 (44)</td>
<td></td>
</tr>
<tr>
<td>25 - 29.9 kg/m²</td>
<td>19 (22)</td>
<td>30 (35)</td>
<td></td>
</tr>
<tr>
<td>≥ 30 kg/m²</td>
<td>20 (23)</td>
<td>18 (21)</td>
<td></td>
</tr>
<tr>
<td>Glucose regulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>4.3 ± 0.3</td>
<td>4.3 ± 0.4</td>
<td>0.780</td>
</tr>
<tr>
<td>Fasting insulin (mU/L)</td>
<td>5.7 ± 3.7</td>
<td>6.0 ± 3.2</td>
<td>0.623</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.1 ± 0.8</td>
<td>1.2 ± 0.7</td>
<td>0.549</td>
</tr>
<tr>
<td>Insulin sensitivity indices (ISI)</td>
<td>9.8 ± 4.6</td>
<td>9. ± 5.2</td>
<td>0.553</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.4 ± 0.3</td>
<td>5.4 ± 0.3</td>
<td>0.427</td>
</tr>
<tr>
<td>Serum C-peptide (nmol/L)</td>
<td>0.35 (0.29 – 0.51)</td>
<td>0.39 (0.29 – 0.52)</td>
<td>0.696</td>
</tr>
</tbody>
</table>

* SEIFA Index of Relative Socio-economic Advantage and Disadvantage (IRSD). Quintile 5 is the relatively most advantaged.
** Other ethnicities include Asians, Eurasians, Hispanics and Polynesians
Figure 3.4. Geographical distribution of participants of The Cycle Study. Women in the EX group are represented by (**) while women in the CON group are represented by (**). The location of The University of Western Australia is represented by (**). The total distance travelled to deliver the exercise intervention was ~ 137,000 km.
3.4.2 Incidence and severity of GDM

The recurrence rate of GDM was similar between groups (Table 3.2). Secondary analysis using the ADIPS (2012) cut off values showed similar recurrence rate of GDM between groups. Likewise, there was no difference in the overall degree of glucose tolerance or insulin response to the OGTT (and the associated area under curve) between groups post-intervention (Figure 3.5). The HOMA-IR and ISI were also similar between groups post-intervention, as was HbA1c and serum C-peptide (Table 3.2). Of the women who were diagnosed with GDM, four women in the control group and one woman in the exercise group required insulin therapy (CON 11.8% vs EX 2.9%; \( P = 0.163 \))

Table 3.2. Gestational diabetes mellitus (GDM) diagnosis, measures of insulin sensitivity and glucose regulations after a 14-week supervised home-based exercise intervention (EX) or standard care (CON) [(means ± SD)/ n (%)/ median(interquartile range)].

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CON (n = 85)</td>
</tr>
<tr>
<td>Diagnosed with GDM</td>
<td>34 (40.0)</td>
</tr>
<tr>
<td>HOMA-IR*</td>
<td>1.25 (0.84 – 2.05)</td>
</tr>
<tr>
<td>ISI**</td>
<td>5.6 (3.9 – 7.8)</td>
</tr>
<tr>
<td>HbA1c (%)***</td>
<td>5.3 ± 0.3</td>
</tr>
<tr>
<td>Serum C-peptide (nmol/L)</td>
<td>0.53 (0.37 – 0.71)</td>
</tr>
</tbody>
</table>

* HOMA-IR, homeostasis model of assessment-insulin resistance.
** ISI, insulin sensitivity indices
***HbA1c, glycosylated haemoglobin
Figure 3.5. Mean (± SE) response of blood glucose and plasma insulin to a 75 g oral glucose tolerance test performed before the intervention (- -◊ - -CON, n = 87; - - ● - -EX, n = 85) and after the intervention (--○--CON, n = 85; --●--EX, n = 84).
3.4.3 Maternal cardiovascular fitness and anthropometrics

Resting HR increased with advancing pregnancy while systolic and diastolic blood pressure remained the same post-intervention. Total cholesterol (HDL and LDL) and triglycerides increased with advancing pregnancy but were not different between groups. Similarly, body mass, sum of skinfolds and girths increased as pregnancy progressed with no difference between groups. Maternal cardiovascular fitness, based on the power output at 75% HR\textsubscript{max} was significantly increased in response to the EX intervention ($P < 0.01$) while it remained unchanged in CON, resulting in higher fitness in EX compared with CON post-intervention ($P < 0.01$). Oxygen consumption at 75% HR\textsubscript{max} remained the stable in CON pre- to post-intervention, but tended to increase in EX following the intervention ($P = 0.05$) (Table 3.3).

3.4.4 Maternal psychological well-being

There were no changes in the EPDS scores over time and no differences between the groups (Table 3.4). Likewise, the number of participants with EPDS scores $\geq 12$ (indicating higher risk for depression in pregnancy) was similar between groups. In contrast, a significant difference in the DASS\textsubscript{21} was noted between CON and EX post-intervention ($P = 0.04$). Social Physique Anxiety Scale scores did not change over time and were similar between groups.
Table 3.3. Maternal health, body anthropometrics and cardiovascular fitness before and after a 14-week supervised home-based exercise intervention (EX) or standard care (CON) (mean ± SD).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre intervention</th>
<th>Post intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CON (n = 87)</td>
<td>EX (n = 85)</td>
</tr>
<tr>
<td>Resting heart rate (bpm)</td>
<td>80 ± 8</td>
<td>78 ± 9</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>106 ± 13</td>
<td>106 ± 11</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>64 ± 9</td>
<td>63 ± 8</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.9 ± 0.8</td>
<td>5.0 ± 0.8</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.7 ± 0.3</td>
<td>1.7 ± 0.3</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.7 ± 0.7</td>
<td>2.8 ± 0.7</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.4 ± 0.6</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td><strong>Maternal anthropometrics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>69.0 ± 16.2</td>
<td>70.5 ± 15.4</td>
</tr>
<tr>
<td>Weight gain (kg) at 28 weeks</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>At birth</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sum of four girth (mm)</td>
<td>157 ± 20</td>
<td>159 ± 19</td>
</tr>
<tr>
<td>Sum of five skinfold (mm)</td>
<td>113 ± 40</td>
<td>122 ± 47</td>
</tr>
<tr>
<td><strong>Cardiovascular fitness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power output_75% HR&lt;sub&gt;max&lt;/sub&gt; (W)</td>
<td>109 ± 21</td>
<td>112 ± 24</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2&lt;/sub&gt;_75% HR&lt;sub&gt;max&lt;/sub&gt; (L/min)</td>
<td>1.50 ± 0.21</td>
<td>1.55 ± 0.29</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2&lt;/sub&gt;_75% HR&lt;sub&gt;max&lt;/sub&gt; (mL/kg/min)</td>
<td>22.5 ± 4.6</td>
<td>22.4 ± 4.7</td>
</tr>
</tbody>
</table>

<sup>a</sup> Indicates a significant main effect for time, P < 0.01
<sup>b</sup> Significant difference between groups post-intervention, P < 0.05
Table 3.4. Maternal psychological well-being assessed through the Edinburgh Postnatal Depression Scale (EPDS), Depression, Anxiety and Stress Scales (DASS\textsubscript{21}) and Social Physique Anxiety Scale (SPAS) before and after a 14-week supervised home-based exercise intervention (EX) or standard care (CON) [(mean ± SD)/ n (%)].

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre intervention</th>
<th>Post intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CON (n = 87)</td>
<td>EX (n = 85)</td>
</tr>
<tr>
<td>EPDS</td>
<td>4.63 ± 3.61</td>
<td>4.44 ± 3.70</td>
</tr>
<tr>
<td>EPDS score ≥ 12</td>
<td>2 (2.3)</td>
<td>5 (5.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DASS\textsubscript{21}</td>
<td>8.17 ± 5.97</td>
<td>8.46 ± 7.19</td>
</tr>
<tr>
<td>SPAS</td>
<td>29.24 ± 11.36</td>
<td>31.34 ± 11.60</td>
</tr>
</tbody>
</table>

\textsuperscript{a} significant difference between groups post-intervention, \( P < 0.05 \)
3.4.5 Daily physical activity levels and nutritional intake

Analysis of daily nutritional intake was not different over time and showed no difference between groups post-intervention in all nutrition variables ($P > 0.05$). There was no difference in physical activity levels and daily nutritional intake at baseline between groups (Table 3.5). As pregnancy progressed, the mean number of steps taken and time spent in light activity decreased while energy expenditure via physical activity and time spent sedentary increased but there was no difference between groups ($P < 0.05$). Time spent in moderate activity was similar over time and showed no difference between groups. However, two of the four exercise habit strength indicators did change differentially across groups. More specifically, scores for patterning of action and exercise automaticity increased significantly from pre-intervention to post-intervention in the EX group ($P < 0.05$) but did not change in the CON group.

3.4.6 Obstetric and neonatal outcomes

There were no differences in any obstetric and neonatal outcomes between groups (Table 3.6). However, there were more male infants born to participants in EX compared with CON ($P < 0.01$). Of note, there was no sex-specific effect of the exercise intervention on birth weight z-score ($P = 0.822$ for male infants; $P = 0.656$ for female infants between EX and CON). Neonate complications included apnoea (CON 1.2%, EX 0%), congenital anomaly (CON 1.2%, EX 1.2%), hypoglycaemia (CON 2.4%, EX 4.6%), jaundice requiring phototherapy (CON 6.9%, EX 3.5%), respiratory problems (CON 6.9%, EX 7.1%), weight loss (CON 2.3%, EX 1.2%) and others such as temperature instability, prematurity and infection (CON 12.6%, EX 7.1%).
Table 3.5. Daily nutritional intake, physical activity levels and exercise behaviour before and after a 14-week supervised, home-based exercise intervention (EX) or standard care (CON) (mean ± SD) (%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre intervention</th>
<th>Post intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daily nutritional intake</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td>7446 ± 1838</td>
<td>7441 ± 1857</td>
</tr>
<tr>
<td>Carbohydrate intake (g)</td>
<td>191 ± 51(43)</td>
<td>187 ± 51 (42)</td>
</tr>
<tr>
<td>Sugar intake (g)</td>
<td>75 ± 29</td>
<td>78 ± 33</td>
</tr>
<tr>
<td>Protein intake (g)</td>
<td>87 ± 24 (20)</td>
<td>90 ± 28 (21)</td>
</tr>
<tr>
<td>Fat intake (g)</td>
<td>69 ± 23 (34)</td>
<td>70 ± 22 (35)</td>
</tr>
<tr>
<td>Saturated fat (g)</td>
<td>27 ± 9</td>
<td>29 ± 9</td>
</tr>
<tr>
<td>Monounsaturated fat (g)</td>
<td>26 ± 10</td>
<td>25 ± 9</td>
</tr>
<tr>
<td>Dietary fibre (g)</td>
<td>23 ± 7</td>
<td>22 ± 11</td>
</tr>
<tr>
<td><strong>Daily physical activity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total steps taken a</td>
<td>6488 ± 1988</td>
<td>6072 ± 1688</td>
</tr>
<tr>
<td>Energy expenditure (kJ) a</td>
<td>1273 ± 605</td>
<td>1289 ± 714</td>
</tr>
<tr>
<td>Time spent sedentary (min) a</td>
<td>1179 ± 81</td>
<td>1182 ± 78</td>
</tr>
<tr>
<td>Moderate activity (min) a</td>
<td>24 ± 14</td>
<td>21 ± 14</td>
</tr>
<tr>
<td><strong>Exercise habit strength</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patterning of action a</td>
<td>20.07 ± 5.65</td>
<td>19.93 ± 5.38</td>
</tr>
<tr>
<td>Automaticity a</td>
<td>20.52 ± 5.65</td>
<td>19.32 ± 5.48</td>
</tr>
<tr>
<td>Stimulus-response bonds</td>
<td>15.97 ± 4.73</td>
<td>16.49 ± 4.98</td>
</tr>
<tr>
<td>Negative consequences for non-performance</td>
<td>16.93 ± 5.82</td>
<td>17.72 ± 6.31</td>
</tr>
</tbody>
</table>

a significant main effect for time (P < 0.01)
b significant difference between groups post-intervention (P < 0.05)
c significant difference within group post-intervention (P < 0.05)
Table 3.6. Obstetric and neonatal outcomes of women randomised to standard care (CON) or a supervised home-based exercise program (EX) [mean ± SD/ n (%)].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CON (n = 85)</th>
<th>EX (n = 84)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset of labour</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>28 (32.9)</td>
<td>25 (29.8)</td>
<td>0.457</td>
</tr>
<tr>
<td>Induced/Augmented</td>
<td>30 (35.3)</td>
<td>33 (39.3)</td>
<td></td>
</tr>
<tr>
<td>No labour</td>
<td>27 (31.8)</td>
<td>26 (31.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Mode of Delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard vaginal delivery</td>
<td>36 (42.4)</td>
<td>38 (45.2)</td>
<td>0.984</td>
</tr>
<tr>
<td>Assisted vaginal delivery</td>
<td>12 (14.1)</td>
<td>11 (13.1)</td>
<td></td>
</tr>
<tr>
<td>Elective caesarean</td>
<td>26 (30.6)</td>
<td>25 (29.8)</td>
<td></td>
</tr>
<tr>
<td>Emergency caesarean</td>
<td>11 (12.9)</td>
<td>10 (11.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Obstetric complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>1 (1.2)</td>
<td>2 (2.4)</td>
<td>0.567</td>
</tr>
<tr>
<td>Retained placenta</td>
<td>1 (1.2)</td>
<td>-</td>
<td>0.319</td>
</tr>
<tr>
<td>Post-partum haemorrhage</td>
<td>2 (2.3)</td>
<td>-</td>
<td>0.660</td>
</tr>
<tr>
<td>Sepsis requiring antibiotics</td>
<td>3 (3.5)</td>
<td>3 (3.5)</td>
<td>0.988</td>
</tr>
<tr>
<td><strong>Neonate outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm labour</td>
<td>5 (5.8)</td>
<td>4 (4.7)</td>
<td>0.711</td>
</tr>
<tr>
<td>Gestational age delivered (wk)</td>
<td>38 ± 2</td>
<td>38 ± 2</td>
<td>0.101</td>
</tr>
<tr>
<td>Apgar score at 5 min &lt; 7</td>
<td>1 (1.2)</td>
<td>2 (2.4)</td>
<td>0.980</td>
</tr>
<tr>
<td>Special care nursery admission</td>
<td>14 (16.5)</td>
<td>8 (9.4)</td>
<td>0.180</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3419 ± 518</td>
<td>3552 ± 469</td>
<td>0.082</td>
</tr>
<tr>
<td>Large for gestational age</td>
<td>10 (11.8)</td>
<td>12 (14.2)</td>
<td>0.336</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>2 (2.4)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Male neonate</td>
<td>35 (41.2)</td>
<td><strong>54 (64.3)</strong></td>
<td>0.003</td>
</tr>
</tbody>
</table>

*significant difference between groups, P < 0.05
3.5 Discussion

This randomised controlled trial examined the effect of a 14-week supervised, home-based exercise program commenced at 14 weeks of pregnancy on the recurrence of GDM and on maternal aerobic fitness, body anthropometrics, and psychological well-being. The exercise intervention did not reduce the recurrence of GDM, nor did it alter the overall degree of glucose intolerance or insulin sensitivity in these women. However, the intervention did elicit improvements in maternal cardiovascular fitness and reduced overall psychological ‘distress’. Importantly, this study has also shown that a program of regular, moderate intensity cycling with brief bouts of elevated exercise intensity is safe during pregnancy, with no detrimental effect on obstetric or neonatal outcomes.

The lack of effect of our intervention on the recurrence of GDM is surprising given the epidemiological data to support a reduction in GDM risk with increasing physical activity (Dempsey, Butler, et al., 2004; Dempsey, Sorensen, et al., 2004; Dye et al., 1997; Tobias et al., 2011), together with experimental studies reporting benefits of regular exercise during pregnancy for glucose tolerance (Barakat et al., 2012; Ong et al., 2009). However, randomised controlled trials investigating the effect of exercise for GDM prevention are limited with conflicting results. Although no previous studies have specifically focused on women with a history of GDM in a previous pregnancy, recent trials in apparently healthy pregnant women have reported no effect of an antenatal exercise intervention (consisting of moderate intensity aerobic, strength and flexibility exercises performed three times a week for 45-60 min) on the incidence of GDM (Barakat et al., 2013; Stafne et al., 2012). In addition, an antenatal exercise intervention aimed at achieving 30 min of moderate intensity physical activity through
self-selected activities was also unable to alter the incidence of GDM in ‘at risk’ women
(Nobles et al., 2015). However, possible limitations to the interpretation of these results
may include commencement of the intervention in the second trimester of pregnancy
when GDM may already be present (83% of women commenced intervention after 14
weeks gestation, Nobles et al., 2015; 18-22 weeks of gestation, Stafne et al., 2012) and
low exercise compliance (62%, Nobles et al., 2015; 55%, Stafne et al., 2012), although
these limitations were not shared by the study of Barakat and colleagues (intervention
commenced from 10-12 weeks gestation with reported compliance > 85%). In contrast,
a recent randomised study by Cordero et al. (2015) reported reduced prevalence of
GDM with a program of land (twice a week) and aquatic-based (once a week) aerobic,
strength and flexibility exercises commenced at 10-14 weeks of pregnancy. Another
study reported reduced risk of GDM in their women in the exercise intervention
compared with the control (Koivusalo et al., 2015), but it was also found that women in
their exercise group showed improved dietary quality.

The commencement time point of the present study was at 14 weeks of pregnancy given
the difficulty of recruiting women to an intervention of this nature any earlier (i.e.
before confirmation of pregnancy at the 12 week ultrasound and associated antenatal
testing). Of relevance, higher pre-pregnancy and early pregnancy physical activity
levels have been reported to be significantly associated with reduced risk of GDM
(Tobias et al., 2010). Indeed, it has been suggested recently that placental function and
gene expression are programmed by the first trimester of pregnancy before changes in
maternal phenotype are noted and before most intervention trials are initiated (Catalano
& deMouzon, 2015). Accordingly, future research could focus on overcoming the
challenges of recruiting earlier in pregnancy and even prior to conception although the
latter would require an extremely large sample size since not all women would continue to pregnancy. In support of this notion, women performing more than 20 min of moderate intensity physical activity (50th percentile) at study entry had a reduced incidence of GDM independent of their group allocation, compared with women performing less than 20 min of daily moderate activity (29% versus 49%; \( P = 0.013 \)). Another point for consideration is that a recent prospective observational study reported that women carrying a male fetus have reduced \( \beta \)-cell function, higher postprandial blood glucose levels, and have an increased risk of GDM (Retnakaran et al., 2015). Of note, the EX group in the present study gave birth to significantly more male infants. Whether this coincidental occurrence influenced the rate of GDM observed in our EX group is not known. On the other hand, the lack of benefit of our intervention for decreasing the recurrence of GDM was unlikely due to low compliance or insufficient exercise intensity. Utilising a one-on-one, fully supervised home-based design, it was ensured that each woman attained an appropriate duration and intensity of exercise and overall compliance to exercise training was excellent (83%). The latter was likely contributed to by removing common barriers to exercise such as issues related to transportation, child care, privacy issues and a lack of time and motivation. Missed sessions were usually due to pregnancy-related symptoms or illness experienced by the participants. It is possible, however, that increasing the frequency of exercise may have altered the results, but this was not feasible because of the logistical requirements of the intervention of this current study. In addition, the specific exercise prescription for preventing GDM remains unclear, although one previous study has reported that low intensity exercise (30% heart rate reserve) may be preferable to vigorous exercise for acutely decreasing capillary glucose concentrations in women at risk of GDM when the duration of exercise is extended beyond 25 min (Ruchat et al., 2012). Thus, the lack of
effect of intervention may be due to the higher intensity of exercise for a duration greater than 25 min. Further research is needed to investigate this issue further. It is also unlikely that the lack of effect of our intervention on GDM was due to compensatory changes in daily nutritional intake given the limited changes observed pre- to post-intervention in both the EX and CON group. Similarly, physical activity levels outside the intervention (i.e. total daily steps and time spent sedentary and in light, moderate physical activity) were similar between groups, implying that neither group compensated for being randomised (or not) to the exercise intervention. However, it is important to note that both groups accumulated >20 min of moderate intensity physical activity on average each day (both pre- and post-intervention). Given that the general population of pregnant women in Australia have been reported to achieve a median of 112.5 min per week (inter-quartile range 44 - 240 min) (Wilkinson, Miller, & Watson, 2009), the sample of women studied here appear to be a more active population.

The level of physical activity of our participants outside of the intervention suggests that the sample of women studied here may not be representative of the general population of pregnant women at risk of GDM. Indeed, 57% of our sample lived in geographic areas of Perth in the top quintile for the Index of Relative Social Advantage and Disadvantage, suggesting economic and social conditions of advantage (Australian Bureau of Statistics, 2013). In addition, the majority of our sample (~80%) had a BMI of < 30 kg/m$^2$ at 13 weeks of pregnancy and were under private obstetric care (72%), another indicator of greater socioeconomic status and education (Australian Bureau of Statistics, 2010), which in turn may influence awareness and commitment to the management of their health status (Gaston & Cramp, 2011; Gouveia et al., 2007).
Furthermore, the willingness of our cohort to volunteer for a 14-week intensive exercise intervention may be indicative of a proactive and diligent approach to avoiding a second GDM diagnosis. In support of this notion, the GDM recurrence rate of 40% observed in each group is substantially lower than the expected recurrence rate based on our hospital data (55%). It is possible that the addition of regular structured exercise training to an already healthy lifestyle does not elicit additional benefits for glucose tolerance and insulin sensitivity. It remains to be determined if contrary results would be obtained in a sample of women that were previously sedentary or would decline to participate in such a randomised intervention. Alternatively, it may be that a short-term exercise program commenced after the first trimester of pregnancy is not sufficient to alter the risk factors for glucose intolerance and GDM. Indeed, a predisposition to GDM may be transgenerational and pre-programmed within their genetic profile over generations (Petry, 2010).

Despite a lack of effect of the exercise intervention on the recurrence or severity of GDM, significant benefits were observed for maternal cardiovascular fitness and psychological well-being following the exercise intervention. The improvement in cardiovascular fitness in EX compared with CON is consistent with other studies which have examined the effects of regular exercise on maternal aerobic adaptations during pregnancy (Collings et al., 1983; Marquez-Sterling et al., 2000; Melzer, Schutz, Soehnchen, et al., 2010; Price et al., 2012; Santos et al., 2005). This increase in fitness is important given the beneficial relationship between maintaining cardiovascular fitness by continuing to exercise during pregnancy and higher levels of fitness and reduced cardiovascular risk factors later in life (Clapp, 2008). Also of importance, the exercise habit strength questionnaire revealed significant increases in the patterning and
automaticity of exercise behaviour within the EX group. These changes were likely a result of the consistent structure and regular repetition of exercise activities undertaken by the EX group, and suggest potential longer-term benefits from the intervention with respect to exercise involvement and adherence. More specifically, increases in habit strength for health behaviours such as exercise make the EX group less reliant on conscious deliberation for execution which in turn increases their probability of occurrence and also makes them more resistant to change (Grove et al., 2014; Lally & Gardner, 2013).

With respect to psychological well-being, the significant reduction in DASS\textsubscript{21} scores in EX but not CON suggests that a home-based program of regular, moderate-to-vigorous exercise can be effective in reducing general psychological distress during pregnancy. This is a potentially important finding because of the documented adverse effects that psychological states such as depression, anxiety and stress can have on development in utero and in infancy/childhood (Diego et al., 2006; Kingston, Tough, & Whitfield, 2012; Schetter & Tanner, 2012). It also highlights the potential value of the DASS\textsubscript{21} for providing information about dimensions of psychological distress during pregnancy that might be overlooked by depression-specific instruments such as the EPDS when assessing populations that fall in the normal range on such measures (Miller, Pallant, & Negri, 2006). Indeed, unlike DASS\textsubscript{21} scores, the EPDS scores were not influenced by the exercise intervention in this study, might have been because there were low levels of depression across-the-board prior to the intervention which left little room for improvement on this measure. Similar “floor effects” may help to explain the lack of change over time in the social physique anxiety measure. Both groups exhibited mean SPA scores below the mid-point (3.5) of the 1-6 response scale at entry, which possibly
reflects a general acceptance of the changes that occur to the body during pregnancy (Skouteris, Carr, Wertheim, Paxton, & Duncombe, 2005).

The lack of effect of the intervention on the obstetric and neonatal outcomes examined here may not be surprising given the lack of effect on glucose regulation and weight gain. The present intervention ceased at 28 weeks of pregnancy to coincide with assessment of the primary outcome measure; however, it is possible that differences may emerge when exercise is continued until delivery. Regardless, the lack of effect of the intervention on the obstetric and neonatal outcomes examined here may provide some further assurance of the safety of regular exercise during the second trimester of pregnancy. Although we have previously shown that a 6-week program of stationary cycling which included brief higher intensity intervals commenced at 28-29 weeks of pregnancy was well-tolerated and did not result in adverse birth outcomes (Halse et al., 2015), this is the first study to utilise self-paced interval exercise over a 14 week period during pregnancy, beginning at 14 weeks of gestation in a large sample of pregnant women. This suggest that self-paced interval exercise may be a suitable exercise prescription for pregnant women since this mode and format of exercise has also been shown to be more enjoyable than traditional continuous exercise (Chapter 2).

In summary, 14-weeks of supervised home-based exercise commenced after the first trimester of pregnancy does not reduce the recurrence of GDM or the degree of decline in glucose tolerance in women with a history of the condition; however, it does benefit maternal fitness and psychological well-being. Future studies should seek to implement exercise interventions earlier in pregnancy and possibly even pre-conception. Given that the women in the present study may not be representative of the general population at
risk of GDM, future studies may also attempt to focus on those women with the lowest health, socioeconomic status and physical activity levels. Finally, regardless of the lack of benefit observed here for the prevention of GDM, the important role of exercise as a management tool following a diagnosis of GDM must be acknowledged (Mottola, 2008).
Chapter 4

General discussion
4.1 Summary

Epidemiological studies have suggested that women who are physically active before and during pregnancy have a reduced risk of developing gestational diabetes mellitus (GDM) (Tobias et al., 2011). Presently, women with healthy, uncomplicated pregnancies are recommended to achieve at least 30 min of moderate intensity exercise on most days of the week (Artal & O'Toole, 2003). However, the specific frequency, duration and intensity of exercise that is required to prevent GDM is not known. In recent years, randomised controlled trials examining the effect of regular antenatal exercise on the prevention of GDM have emerged in the literature, although results have been inconclusive. A potential limitation for some of these studies is low compliance to exercise interventions. Furthermore, no studies have specifically focused on women with a history of GDM in a previous pregnancy who are at high risk of recurrence. Therefore, the primary aim of this thesis was to determine the effectiveness of a 14-week supervised, home-based exercise program for the prevention of GDM, in a sample of women with a history of GDM in a previous pregnancy. The supervised, home-based nature of this intervention was intended to overcome the issues of transportation and the need for childcare arrangements in order for a mother to engage in exercise, while the provision of a qualified exercise professional was intended to motivate women to commence (and continue) exercise. This is important given that fewer than half the number of pregnant women achieve the recommended levels of physical activity during pregnancy (de Jersey et al., 2013; Evenson & Wen, 2010). This is despite most women understanding the benefits of exercise during pregnancy and that it is safe and appropriate to begin an exercise program during pregnancy (Evenson & Bradley, 2010).
Before addressing the primary aim of this thesis, it was important to consider the type of exercise to be incorporated into a 14-week program of regular stationary cycling during pregnancy which can maximise energy expenditure and enhance enjoyment of the activity. Given the potential for interval exercise as a means to incorporate some vigorous exercise into a moderate intensity exercise routine, and its prior use in a pregnant population showing no detrimental effects (Halse et al., 2015), this format of exercise was considered. However, it was not known if the addition of brief, higher intensity periods to continuous stationary cycling exercise would compromise enjoyment in this population while increasing energy expenditure. Given the importance of enjoyment of exercise for encouraging engagement and adherence to exercise during pregnancy, a secondary aim of this thesis was to examine how the addition of brief, self-paced, higher intensity intervals to traditional continuous moderate intensity exercise affects energy expenditure and the enjoyment of exercise in pregnant women. The outcomes of these research aims were intended to provide further insight regarding the prescription of exercise for preventing GDM.

4.2 Conclusions

Overall, this thesis has shown that:

- A 30-min session of interval stationary cycling, consisting of brief periods of elevated intensity and sufficient recovery at moderate intensity is well tolerated and rated as more enjoyable by women in the third trimester of pregnancy compared with a session of traditional continuous moderate intensity cycling alone.
• The addition of as little as six 15-s higher intensity intervals (90 s in total) to 20 min of continuous moderate intensity cycling significantly increased exercise energy expenditure by 28%.

• A 14-week supervised, home-based interval stationary cycling exercise program performed during the second trimester of pregnancy, up until the diagnosis of GDM did not reduce the recurrence of GDM, or the degree of decline in glucose tolerance in women with a history of the condition in a previous pregnancy.

• A 14-week supervised, home-based interval stationary cycling exercise program commenced after the first trimester of pregnancy did not reduce the recurrence of GDM or the degree of decline in glucose tolerance in women with a history of the condition in a previous pregnancy.

• A 14-week supervised, home-based exercise program commenced after the first trimester of pregnancy does benefit maternal cardiovascular fitness and psychological well-being in women with a history of GDM.

• A 14-week supervised, home-based interval stationary cycling exercise program commenced after the first trimester of pregnancy is safe and does not adversely affect obstetric and neonatal outcomes.

4.3 Implications

If the rising incidence of GDM is not prevented, the serious and lifelong health implications for women and their children affected by a GDM pregnancy will continue
to add to the epidemic of metabolic issues faced by today’s society. Despite epidemiological evidence supporting a role for exercise to prevent GDM, the evidence from randomised, controlled trials is limited. The findings of this thesis suggest that an antenatal program of supervised, home-based exercise commenced at 14 weeks of pregnancy was ineffective in preventing GDM in ‘at-risk’ women with a history of the condition in a previous pregnancy (Chapter 3). Although no previous studies have specifically focused on a population of women with a history of GDM in an earlier pregnancy, the observation that an exercise intervention commenced after the first trimester of pregnancy does not prevent GDM is consistent with several other studies (Barakat et al., 2013; Nobles et al., 2015; Stafne et al., 2012). It is possible that future exercise interventions need to commence in early pregnancy (i.e. in the first trimester) or even during the pre-conception period before the metabolic phenotype is programmed. Alternatively, the lack of effect of exercise interventions may be indicative of a complex pathophysiology of GDM that is unaffected by changes in physical activity levels, or that GDM is non-responsive to short-term exercise interventions and instead requires a life-course approach to prevent this condition.

Despite no effect of the exercise program on GDM recurrence, the beneficial effects of a 14-week, thrice weekly cycling program on maternal cardiovascular fitness and psychological well-being supports the importance of achieving recommended levels of physical activity during pregnancy. In addition, this thesis has demonstrated that a regular program of interval-type stationary cycling is safe and well tolerated during pregnancy, with no adverse effects on maternal and neonatal pregnancy outcomes. Furthermore, the benefit of the exercise intervention for psychological well-being
reported in this thesis may highlight a promising strategy to tackle perinatal mental health issues faced by one in five mothers of young children (AIHW, 2012).

Of relevance, the barriers to exercise for the pregnant population include a lack of time, availability and cost of child care, as well as concerns about the safety of exercise in pregnancy (Evenson et al., 2009). In an attempt to address these barriers, stationary cycling was chosen as the exercise modality for this thesis as it can be readily applied to the population of pregnant women with existing children regardless of weather conditions and performed in the comfort of their own home; simultaneously removing pregnancy-specific exercise limitations that are made worse by load-bearing movements (such as walking), as well as problems related to child care requirements. Given that the 14-week exercise intervention presented in this thesis achieved a high compliance rate (83%), this suggests that the supervised, home-based nature was successful in overcoming barriers to exercise, making exercise a possibility for this busy, time-poor population. The exercise intervention utilised an interval training format based on the findings from Chapter 2 showing that pregnant women (n = 12) found it more enjoyable to perform add brief higher intensity bouts to their continuous moderate intensity cycling sessions, despite the performance of more total work and higher overall energy expenditure. The added enjoyment of exercise provided by this form of tempered interval training may have contributed to the high compliance reported in Chapter 3, although it has not been examined whether a supervised, home-based exercise program of traditional steady-paced continuous aerobic exercise would result in the same compliance.
4.4 Limitations and directions for future research

Although the results and conclusions arising from this thesis have important implications, the following limitations are apparent, requiring further research to address them.

4.4.1 Chapter 2: Interval-type exercise for the pregnant woman

- The application of the results cannot be generalised to all pregnant women because the sample was limited to 12 healthy, recreationally active pregnant women in the last trimester of pregnancy. As such, the physiological and psychological responses to interval-type exercise and continuous moderate intensity exercise need to be examined over various time points during pregnancy to identify whether the findings of this study are applicable over the course of a woman’s pregnancy.

- The ratings of the enjoyment of exercise were based on only two acute exercise sessions. It is possible that the regular performance of interval-type exercise compared with traditional continuous exercise may result in different enjoyment levels. Future research may compare enjoyment levels and adherence rates between a regular program of interval-type exercise and a regular program of traditional continuous moderate intensity exercise.

- Only one particular protocol of interval exercise (the addition of six, 15-second self-paced sprints repeated every 2 min 45 s throughout a 20-min condition phase) was examined. The options for interval exercise are numerous and future research may examine other protocols to optimise energy expenditure and
enjoyment to enhance cardiovascular benefits and exercise adherence in pregnant women.

- The exercise modality (i.e. walking, cycling or swimming) may affect the enjoyment level of interval-type exercise performed in pregnancy. Only stationary cycling was examined in the present study.

- Fetal responses to the exercise trials were not monitored. Given the novelty of applying interval-type exercise to the pregnant population, future research may consider assessing acute fetal responses to this form of exercise. This information could provide further support for the use of this type of exercise during pregnancy.

4.4.2 Chapter 3: Can regular exercise in pregnancy prevent GDM?

- The intervention was commenced in the second trimester of pregnancy. As it has been recently suggested that placental function and gene expression are programmed by the first trimester of pregnancy before changes in maternal phenotype (Catalano & deMouzon, 2015), our intervention may have commenced too late. However, it was unrealistic to commence the intervention any earlier in pregnancy, as most women have their first visit with their obstetrician only after learning of their pregnancy (and for some this may be towards the end of their first trimester). Future studies may endeavour to recruit women earlier in pregnancy, or even in the preconception period, although the sample size require for such a study would be much larger than the current study making the feasibility of conducting a similar type of home-based intervention a
challenge. On the other hand, as the intervention concluded at the time of routine testing (28 weeks of gestation), there was no data on the effect of exercise on the outcome variables should the cycling had continued until delivery. However, it is likely that benefits for glycaemic control would have been observed should the intervention had continued up to delivery, given the result of the study by Halse and colleagues (2014).

- The voluntary nature of this randomised controlled trial meant that the population of women studied in this thesis may not be representative of the general population of women at risk of GDM. In particular, sedentary women of lower socioeconomic status might have more to benefit from a supervised, home-based exercise intervention. Future studies could consider promoting the potential benefits of participating in such trials so to raise awareness in the lower socioeconomic group of women prior to recruitment. This could foster a larger and more diverse population of pregnant women from different backgrounds.

- Another limitation of our study was the intensive nature and high cost involved in delivering a supervised home-based exercise intervention. The one-on-one nature of the intervention was labour intensive which implies that application to the general population would require generous government funding or support from private investors. This made it impossible to deliver the exercise intervention as a four or five day exercise program, which may have affected the diagnosis of GDM. Future studies could accommodate a large sample size by shifting the focus from one-on-one training towards community-based exercise sessions conducted over multiple centres. Alternatively, a combination of the
supervised, home-based nature of our intervention with the use of current technological advances may reduce the labour intensity nature and cost of the intervention. For example, real time video conferencing for the duration of the exercise session or computerised exercise equipment that can log the duration and intensity of exercise sessions in the absence of supervision could transfer accountability to exercise compliance towards the participant instead of the heavy reliance on a visiting exercise physiologist.

- This study monitored participants up to the point of labour and birth. While there were no significant differences in obstetric and neonate outcomes between the exercise and control group, it is not known if participation in our exercise intervention influenced the future life-course of the child. Future research could involve follow-up of the children of our study population to determine any effects of the intervention on their physical and cognitive development to assess the impact of exercise in pregnancy on future generations.
References
References


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Appendix A

Participant information sheet & consent forms
Continuous versus intermittent stationary cycling in late pregnancy: a comparison of energy expenditure and enjoyment
- Participant Information Sheet-

Purpose of this study:
Stationary cycling is a recommended mode of exercise for women with healthy pregnancies. However, the best type of exercise to perform on a stationary bike during pregnancy is not known. Intermittent/interval exercise is becoming more popular because it allows for higher energy expenditure in the same amount of time performing exercise at a continuous pace. The aim of this study is to compare the body’s responses to continuous and intermittent stationary cycling during pregnancy. Responses of interest include the amount of energy expended, heart rate, the levels of lactate and glucose in the blood, feelings of exertion and enjoyment. By establishing the type of exercise that is most enjoyable during pregnancy, the outcomes of this study could assist health and fitness professionals in formulating an exercise program that pregnant women will continue to engage in throughout their pregnancies.

Overview
You are invited to participate in this study to determine the responses to cycling continuously at a moderate intensity with short bouts of higher intensity cycling compared with a session of continuous cycling at a constant rate alone. Should you choose to volunteer, you will be required to attend 3 laboratory sessions at the School of Sport Science, Exercise and Health over 2 weeks of your pregnancy. The first visit is a 1-hour familiarization session in which you will be informed about the study and what will be required of you. During this session we will ask that you complete a questionnaire related to your readiness for exercise in pregnancy and preferences and tolerance to exercise intensity (which will take approximately 20 minutes in total). We will also take measures of your weight and height and measure your fitness levels using the Tri-level fitness. A Tri-level fitness test is a submaximal (moderate) aerobic fitness test conducted on a stationary bike which normally takes 4-5 minutes in total and is shown to be safe for pregnant woman. The test begins with cycling at a leisurely pace. With each passing minute, you will be required to cycling more intensely until your heart rate reaches 75% of your age-predicted maximum (calculated by taking 220 - (your age) x 0.75). During the cycling, you will wear a special belt around your chest to record how fast your heart is beating and you will also breathe into a mouthpiece to allow us to collect your expired air to work out how much
oxygen your body is using. From this test, we will work out what level you will exercise at in the next two visits.

The two laboratory sessions following this, will be scheduled at a similar time in the morning within a 2-week period, at least 2-days apart. Each session will take no more than 1.5 hours, which includes a 30-minute session of cycling.

On your arrival to the laboratory at each session, you will be requested to answer a couple of short questions on your fatigue levels and feelings of the impending exercise session. At each laboratory visit, you will take part in one of the following sessions:

- A 30-minute cycling session at a moderate intensity continuous pace (as determined by the Tri-level fitness test)
- A 30-minute cycling session at moderate intensity continuous pace; with 6 periods of higher intensity cycling (no more than 15 seconds)

During the exercise, we will require you to answer questionnaires on your thoughts about the cycling session and to rate your perceived level of exertion. Once again, you will wear a special belt around your chest to allow us to monitor your heart beat per minute during exercise. You will also be breathing through a mouthpiece as you did for the Tri-level fitness test. To monitor the exercise intensity, you will be asked of your rate of perceived exertion at 5-min time points and asked your level of enjoyment at 15-min and 30-min time points of the exercise. During the course of each laboratory session we will take three small capillary blood samples taken from your fingertip (less than one tenth of a milliliter). This involves a small prick on the fingertip with a sterile lancet device. You may experience slight discomfort with the procedure, however this is only temporary. Of note, you can request to stop exercise at any point during the sessions if you are feeling unwell.

**Risks:**
Thirty minutes of moderate intensity exercise on most days of the week is recommended for women with no pregnancy complications. However, while it is very uncommon, bouts of exercise in the final trimester of pregnancy may trigger the onset of labour. Should this happen to you, please contact your obstetrician immediately and seek medical attention promptly.

**Confidentiality:**
Your confidentiality will be maintained throughout the study through random assignment of a number to de-identify your data. All data collected will be securely stored in a locked filing cabinet and password-protected computer assessable only to the chief investigator and PhD student (MJ Ong). The findings of this study may be published, however all information used will be non-identifiable.
Your Rights:
Participation in this research is voluntary and you are free to withdraw from the study at any time without prejudice. You can withdraw for any reason and you do not need to justify your decision. If you withdraw from the study and you are an employee or student at the University of Western Australia (UWA) this will not prejudice your status and rights as employee or student of UWA. If you do withdraw we may wish to retain the data that we have recorded from you but only if you agree, otherwise your records will be destroyed.
Your participation in this study does not prejudice any right to compensation that you may have under statute of common law. If you have any questions concerning the research at any time please feel free to contact PhD candidate, MJ Ong, on mobile 0403 145 680 or email 10449515@student.uwa.edu.au. Further information regarding this study may be obtained from Associate Professor Kym Guelfi on 6488 2602 or kym.guelfi@uwa.edu.au.

The Human Research Ethics Committee at the University of Western Australia requires that all participants are informed that, if they have any complaint regarding the manner, in which a research project is conducted, it may be given to the researcher or, alternatively to the Secretary, Human Research Ethics Committee, Registrar’s Office, University of Western Australia, 35 Stirling Highway, Crawley, WA 6009 (telephone number 6488-3703). All study participants will be provided with a copy of the Information Sheet and Consent Form for their personal records.
Continuous versus intermittent stationary cycling in late pregnancy: a comparison of energy expenditure and enjoyment

— Consent Form —

I ___________________________ have read the information provided and any questions I have asked have been answered to my satisfaction. I agree to participate in this activity, realising that I may withdraw at any time without reason and without prejudice.

I understand that all information provided is treated as strictly confidential and will not be released by the investigator unless required to by law. I have been advised as to what data is being collected, what the purpose is, and what will be done with the data upon completion of the research.

I agree that research data gathered for the study may be published provided my name or other identifying information is not used.

______________________                    __________________
Participant                                             Date

The Human Research Ethics Committee at the University of Western Australia requires that all participants are informed that, if they have any complaint regarding the manner, in which a research project is conducted, it may be given to the researcher or, alternatively to the Secretary, Human Research Ethics Committee, Registrar’s Office, University of Western Australia, 35 Stirling Highway, Crawley, WA 6009 (telephone number 6488-3703). All study participants will be provided with a copy of the Information Sheet and Consent Form for their personal records.
Continuous versus intermittent stationary cycling in late pregnancy: a comparison of energy expenditure and enjoyment

The School of Sports Science, Exercise and Health is conducting a research study that aims to examine the responses to continuous and interval-type stationary cycling during pregnancy.

This study will require you to attend three laboratory sessions over 2 weeks of your pregnancy. Each session will last 1 to 1.5hr.

If you are currently 28 - 30 weeks pregnant with no existing complications, and would like to learn more about how your body responds to exercise in your last trimester of pregnancy, please contact MJ Ong on 0403 145 680 or email mj.ong@research.uwa.edu.au
The Cycle Study

A study of the effectiveness of cycling exercise in breaking the cycle of pregnancy diabetes

BACKGROUND

Diabetes is a common medical complication of pregnancy and may cause serious health problems for both the mother and her baby. These problems can occur before, during and after birth. If blood sugar levels are not controlled, the baby may become large, making the birth more difficult and leading to problems with the baby controlling their blood sugars in the early newborn period. These babies also have a higher risk of obesity and developing diabetes later in life. For the mother, there is increased risk of high blood pressure and injury to the birth canal during delivery, as well as increased future risk of diabetes, requiring lifelong management. Although regular exercise offers many benefits for both the mother and child, it is not known whether it can prevent gestational diabetes, especially in women with a previous history of the condition. Therefore, the aim of this study is to examine the effect of 14 weeks of supervised home-based exercise (commenced at 14 weeks of pregnancy) on the recurrence of gestational diabetes, along with other aspects of wellbeing for the mother and child. If shown to be beneficial, this program will have profound benefits for women, their children, and future generations.

PRIOR SCIENTIFIC RESEARCH

Over the past 20 years, there has been much research on the potential benefits and safety of exercise for both mother and baby during pregnancy. Regular exercise during pregnancy has been shown to help women stay mobile, manage their weight, as well as improve self-esteem and mental health. There is also some evidence that regular exercise decreases the risk of diabetes during pregnancy. However, no studies have assessed whether regular exercise can prevent gestational diabetes in women with a history of the condition in a previous pregnancy.

THE IMPORTANCE OF THIS STUDY

In order for us to find out whether regular exercise can reduce the risk of a woman developing gestational diabetes during pregnancy, we would like you to be a part of our very important research. If shown to be effective, regular exercise can be used for future pregnancies in Western Australia to benefit both mother and child. Whilst your consent and participation in this study may or may not benefit your pregnancy, the results may contribute to the development of improved guidelines for exercise during pregnancy.
THE PROGRAM

Being involved in the study means you will be randomly allocated to either an exercise program or encouraged to maintain your usual level of activity. If you are allocated to the exercise program, you will complete 14 weeks of home-based personal exercise (three, 30-60 minute sessions per week). All exercise sessions will be completed in the comfort of your own home on a stationary bike and fully supervised by qualified professionals from the School of Sports Science, Exercise and Health at The University of Western Australia. **The cycling program will run from 14 weeks of your pregnancy until approximately 27 weeks of your pregnancy.**

If you are not allocated to the exercise program, you will not complete the home-based exercise program and will continue with your normal activity throughout the 14 week period (i.e. 14 weeks to 27 weeks gestation). Participation in this program will not alter the management of your pregnancy by King Edward Memorial Hospital and all women will continue to receive regular antenatal care, together with the tests outlined below at the start (14 weeks of pregnancy) and end of the study (28 weeks of pregnancy).

THE TESTS

If you agree to participate in this study, you will be required to complete the following tests at the start of the study (13 weeks of pregnancy) and again at the end of the study (28 weeks).

**Session 1** will take place at the School of Sports Science, Exercise and Health at The University of Western Australia (please see attached map). During this visit, your fitness levels will be measured by completing approximately five minutes of submaximal (moderate) cycling on a stationary bike. During the cycling, you will wear a special belt around your chest to record how fast your heart is beating and you will also breathe into a mouthpiece to allow us to collect your expired air to work out how much oxygen your body is using. After the short fitness test, we will record your height, weight and other body measures (i.e. waist and limb girths and skinfold thickness). Then you will be required to complete some questionnaires about your mobility during pregnancy and general health and well-being. This visit will take approximately 1 hour in total. When you are finished, you will be given a small device on a belt (called an accelerometer) to wear around your waist at the level of the hip for the next seven days. This small device will record your activity/movement levels. In addition, you will be given a food diary to record your food and drink intake for the next seven days. At this session, you will be given a Pathwest blood form for **Session 2** (See below).

**Session 2** will take place at a PathWest Centre most convenient to you (centres are located all around Perth). For this visit, you will need to arrive fasted in the morning (meaning no food or drink except water for ~10 hours prior i.e. since the evening before). Upon arrival you will complete an oral glucose tolerance test. This involves a fasting blood test followed by the consumption of a sugar drink and having regular blood samples taken (at 30, 60, 90 and 120 minutes) from a vein near the crease of your elbow to see how your body responds to the drink. Glycosylated haemoglobin (a measure of the average amount of sugar in your blood), C-peptide and blood cholesterol levels will also be measured. This visit will take a maximum of 2.5 hours. It is important to note that the oral glucose tolerance test at 28 weeks of gestation is part of your normal care routine and only the test at 14 weeks of gestation is additional to routine care.
DATA COLLECTION

All of the data collected throughout the project will be de-identified and stored securely on a computer database in code. Only the investigators involved with the study will have access to the information. At the end of your pregnancy some clinical information will be collected from your medical records including how your pregnancy and labour went and how the baby was after delivery. Again all of this information will be de-identified and coded into the computer database.

QUESTIONS?

If you have further questions about the study, please contact the Chief Investigator Professor John Newnham on 9340 1331 or via email at john.newnham@uwa.edu.au. If you have any concerns or complaints regarding this study, you can contact the Director of Medical Services at KEMH on 9340 2222. Your concerns will be drawn to the attention of the Ethics Committee who is monitoring the study. This person is not involved with the research project in any way and calling them will not affect your participation in the study.

THANK YOU FOR YOUR TIME
Appendix B

Chapter 2 Data collection sheets
**Participant information**

<table>
<thead>
<tr>
<th>Name</th>
<th>Assigned ID</th>
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**Anthropometric Measures**

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<th>Blood Pressure</th>
<th>RHR</th>
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**Questionnaires**

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<table>
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<tr>
<th>Sleep (hrs)</th>
<th>How energised are you?</th>
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**Aerobic Power Index**

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<th>Time (min)</th>
<th>Power Output Target/Actual</th>
<th>HR</th>
<th>O2</th>
<th>75% HRmax (aged-predicted)</th>
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<tr>
<td>2</td>
<td>25W</td>
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<td>4</td>
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<td>Calculations</td>
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<td>75W</td>
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<td>8</td>
<td>100W</td>
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<td>10</td>
<td>125W</td>
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<td>12</td>
<td>150W</td>
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<td>14</td>
<td>175W</td>
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Intensity of exercise trials

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<tr>
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<tbody>
<tr>
<td>Continuous</td>
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**Interval**

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<td>Appointment 1</td>
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<tr>
<td>Appointment 2</td>
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Please remember to write down the food items you eat for the morning before the first appointment. We will be reminding you to consume the same type and quantity of breakfast for the second appointment.

Please bring this food recall on the day of your second appointment.

<table>
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</tbody>
</table>
#Sprint on every 3 minutes. “For the next 15 seconds, pedal faster to increase your cycling effort as much as you feel you can.”
Please rate how you feel about the exercise you just performed.

<table>
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<tr>
<th>Question</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<tr>
<td>I enjoy it</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I feel bored</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>I dislike it</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I find it pleasurable</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>I am very absorbed in this activity</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>It is no fun at all</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>I find it energizing</td>
<td></td>
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<tr>
<td>It makes me depressed</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>It is very unpleasant</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It feels good physically when I am doing it</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is very invigorating</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is very exciting</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>It is not at all simulating</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>I am very frustrated by it</td>
<td></td>
<td></td>
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<tr>
<td>It gives me a strong sense of accomplishment</td>
<td></td>
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<tr>
<td>It is very refreshing</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I would rather be doing something else</td>
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</table>
### Responses to exercise trials

<table>
<thead>
<tr>
<th>Did you prefer the continuous or intermittent exercise trial? (please circle)</th>
<th>Continuous</th>
<th>Intermittent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Why?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If it was a 3-month cycling program, where you will need to perform 3 sessions of cycling per week, would you prefer performing continuous cycling sessions or intermittent cycling sessions? (please circle)</th>
<th>Continuous</th>
<th>Intermittent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Why?</td>
<td></td>
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Appendix C

Chapter 3 Data collection sheets
<table>
<thead>
<tr>
<th>Gestation</th>
<th>Date</th>
<th>Action</th>
<th>By</th>
<th>Done?</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td></td>
<td>Recruited</td>
<td>Cherry</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>Make contact with recruit and organise first appointment</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>Send reminder text or phone call</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>Baseline Assessment &amp; Randomisation</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arrange for appointment to pick up accelerometer &amp; food diary (if assigned control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>After 2 days - call to check pathology appointment &amp; reminder of accelerometer/food diary procedures</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Confirm Blood Results with Cherry before bike delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>Issue Training Compliance Sheets to Trainer</td>
<td>MJ &amp; Trainer (LJ)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bike Delivery &amp; First Session Induction</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Pick up accelerometer &amp; food diary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>Obtain Blood Results from Kym</td>
<td>MJ &amp; Kym</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>Send Assessment Report to participant</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Obtain update from Trainer Call Control for catch up</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td></td>
<td>Obtain update from Trainer Call Control for catch up</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>Obtain update from Trainer Call Control for catch up</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Remind participant &amp; doctor of the Blood Forms to use</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td>Obtain update from Trainer Call Control for catch up</td>
<td>MJ</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Remind trainer this is last week of training</td>
<td>MJ &amp; Trainer (LJ)</td>
<td></td>
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<tr>
<td>27</td>
<td></td>
<td>Organise last session bike collection</td>
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<td>Collect Training Compliance Sheets from Trainer</td>
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<tr>
<td>28</td>
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<td>Post Intervention Assessment</td>
<td>MJ</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Send out Thank you letter &amp; Assessment Report</td>
<td>MJ</td>
<td></td>
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<tr>
<td>Post Delivery</td>
<td></td>
<td>Remind Cherry to collect post delivery data</td>
<td>MJ</td>
<td></td>
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</tbody>
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### Participant Details

<table>
<thead>
<tr>
<th>First Name</th>
<th>Surname</th>
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<table>
<thead>
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<th>No of children:</th>
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<table>
<thead>
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<th>Home Address</th>
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<table>
<thead>
<tr>
<th>Phone</th>
<th>(mobile)</th>
<th>(home)</th>
<th>(work)</th>
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<tbody>
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<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Aboriginal</th>
<th>Caucasian</th>
<th>Asian</th>
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<table>
<thead>
<tr>
<th>When was the last time you smoked?</th>
<th>Never smoked</th>
<th>Years:</th>
<th>Months:</th>
<th>Days:</th>
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### Participant Birthing Information

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<th>Based on</th>
<th>Ultrasound</th>
<th>LMP</th>
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<table>
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<tr>
<th>Recruited at</th>
<th>Armadale</th>
<th>Joondalup</th>
<th>KEMH</th>
<th>Rockingham</th>
<th>OPCH</th>
<th>Swan</th>
<th>Other</th>
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If other, please specify:

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<tr>
<th>Delivering at</th>
<th>KEMH</th>
<th>Other:</th>
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### Partner Contact Details

<table>
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<th>Surname</th>
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<table>
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<th>(home)</th>
<th>(work)</th>
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### Additional Contact Details

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<table>
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<table>
<thead>
<tr>
<th>Home Address</th>
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<table>
<thead>
<tr>
<th>Phone</th>
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<th>(home)</th>
<th>(work)</th>
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### Doctor’s Contact Details

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<th>(mobile)</th>
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## Participant Information

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<table>
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<tr>
<th>DOB / Age</th>
<th>Weeks of Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resting HR (bpm)</th>
<th>Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Anthropometric Measurements

<table>
<thead>
<tr>
<th>Height (cm)</th>
<th>Body Mass (kg)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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</tr>
</tbody>
</table>

**Girths (cm) *must obtain two readings**

<table>
<thead>
<tr>
<th>Relaxed Arm</th>
<th>Flexed Arm</th>
<th>Thigh</th>
<th>Calf</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

**Skinfold (mm) *must obtain two readings**

<table>
<thead>
<tr>
<th>Triceps</th>
<th>Subscapular</th>
<th>Biceps</th>
<th>Thigh</th>
<th>Calf</th>
<th>Sum of 5 SF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Maternal Aerobic Fitness

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Power (Watts)</th>
<th>Heart rate (bpm)</th>
<th>(O_2) consumption (L/min)</th>
<th>Seat Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>100</td>
<td></td>
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<tr>
<td>10</td>
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</tr>
</tbody>
</table>

**Seat Height**

<table>
<thead>
<tr>
<th>Bike used</th>
<th>Meta Cart</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA04</td>
<td></td>
</tr>
</tbody>
</table>

**Heart Rate & Power Output Calculations**

\[ \text{Target HR (75\% HRmax)} = (220 - \text{age}) \times 0.75 \]

<table>
<thead>
<tr>
<th>Final HR</th>
<th>Second last HR</th>
<th>Final power output</th>
<th>Second last power output</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Oxygen Consumption Measures**

<table>
<thead>
<tr>
<th>Final (O_2) consumption (L/min)</th>
<th>Second last (O_2) consumption (L/min)</th>
<th>(O_2) consumption at Target HR: (L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data Sheet</td>
<td>14-Week Assessment</td>
<td></td>
</tr>
</tbody>
</table>

### Dietary Analysis - Food Works

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy intake per day (kJ)</td>
<td></td>
</tr>
<tr>
<td>% carbohydrate intake</td>
<td></td>
</tr>
<tr>
<td>% fat intake</td>
<td></td>
</tr>
<tr>
<td>% protein intake</td>
<td></td>
</tr>
</tbody>
</table>

### Physical Activity Levels - Accelerometer

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Counts per day</td>
<td>Steps per day</td>
</tr>
<tr>
<td>Time Sedentary (min/day)</td>
<td>Time Light PA (min/day)</td>
</tr>
<tr>
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<td>Time Heavy PA (min/day)</td>
</tr>
<tr>
<td>Total Caloric Output</td>
<td></td>
</tr>
</tbody>
</table>

### Bloods

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Form has been issued to participant?</td>
<td></td>
</tr>
<tr>
<td>Letter to participant’s doctor provided?</td>
<td></td>
</tr>
<tr>
<td>Remarks?</td>
<td></td>
</tr>
</tbody>
</table>

### Randomisation

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>EXERCISE</td>
<td>CONTROL</td>
</tr>
</tbody>
</table>

### Appointment for accelerometer and food diary collection / bike delivery

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td></td>
</tr>
</tbody>
</table>

### Additional Notes

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
## Participant Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Name of Tester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study #</th>
<th>Date of Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DOB / Age</th>
<th>Weeks of Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Resting HR (bpm)</th>
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<table>
<thead>
<tr>
<th>Bicep</th>
<th>Thigh</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
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<table>
<thead>
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**Heart Rate & Power Output Calculations**

Target HR (75% HRmax) = (220 - age) x 0.75

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</tbody>
</table>

**Oxygen Consumption Measures**

- Final O₂ consumption ...........L/min
- Second last O₂ consumption ...........L/min
- O₂ consumption at Target HR: ...........L/min

<table>
<thead>
<tr>
<th></th>
<th>Power output at Target HR: ...........watts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Power output at Target HR: ...........watts/kg</td>
</tr>
</tbody>
</table>
### Dietary Analysis - Food Works

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<table>
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### Physical Activity Levels - Accelerometer

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<table>
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</thead>
<tbody>
<tr>
<td>Form has been issued to participant?</td>
<td></td>
</tr>
<tr>
<td>Remind participant’s doctor regarding blood forms provided?</td>
<td></td>
</tr>
<tr>
<td>Remarks?</td>
<td></td>
</tr>
</tbody>
</table>

### Birth Centre and Delivery Date

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Centre</td>
<td></td>
</tr>
<tr>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Remind Cherry as date draws near</td>
<td></td>
</tr>
</tbody>
</table>

### Additional Notes

|   |   |
Please record all food and drinks that you have for the next 7 days on the form provided. You should write the food and drinks down as soon as you have them. At a minimum you will need to fill in the form at the end of each day. For all food and drinks that you eat, please record as many details as possible including:

- the **type** of food (i.e. full cream milk or hilo or skim)
- the **amount** (grams / mL / number of pieces) of each food/drink
- the **brand** name if possible
- the **way that the meal was cooked** (i.e. grilled versus deep fried)

Below is an example.

<table>
<thead>
<tr>
<th>Meal</th>
<th>Food Type (e.g. wholegrain bread, vegemite)</th>
<th>Brand (e.g. Mias, Kraft)</th>
<th>Cooking method (or other comments)</th>
<th>Amount (in grams or mL or number of pieces)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BREAKFAST</td>
<td>Wholegrain bread</td>
<td>Woolworths</td>
<td>Toasted</td>
<td>4 slices</td>
</tr>
<tr>
<td></td>
<td>Orange Juice</td>
<td>Brownes Orange C</td>
<td></td>
<td>2 cups</td>
</tr>
<tr>
<td></td>
<td>Vegemite spread</td>
<td>Vegemite</td>
<td></td>
<td>½ tablespoon</td>
</tr>
<tr>
<td>LUNCH</td>
<td>Multigrain roll</td>
<td>Local bakery</td>
<td>Medium size</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ham</td>
<td>Deli item</td>
<td>3 thick cut slices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cheddar cheese</td>
<td>Kraft slices</td>
<td>2 thin slices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grated carrot</td>
<td></td>
<td></td>
<td>1 cup</td>
</tr>
<tr>
<td></td>
<td>Beetroot</td>
<td></td>
<td></td>
<td>2 slices</td>
</tr>
<tr>
<td></td>
<td>Choc milk</td>
<td>Masters</td>
<td></td>
<td>600 ml</td>
</tr>
<tr>
<td>DINNER</td>
<td>Steak</td>
<td>Coles</td>
<td>BBQ cooked</td>
<td>350 g</td>
</tr>
<tr>
<td></td>
<td>Potatoes</td>
<td></td>
<td>baked</td>
<td>2 baby/small</td>
</tr>
<tr>
<td></td>
<td>Garden Salad + dressing</td>
<td>Homemade</td>
<td></td>
<td>2 x cups salad 1 tablespoon dressing</td>
</tr>
<tr>
<td></td>
<td>Choc chip ice cream, low fat</td>
<td>Nestle</td>
<td></td>
<td>3 med. scoops</td>
</tr>
<tr>
<td></td>
<td>Water</td>
<td></td>
<td></td>
<td>3 cups (750 mL)</td>
</tr>
<tr>
<td>SNACKS</td>
<td>Low fat milk</td>
<td>Brownes</td>
<td></td>
<td>1 cup (300 mL)</td>
</tr>
<tr>
<td></td>
<td>Banana muffin</td>
<td>homemade</td>
<td>Medium size</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mixed nuts</td>
<td></td>
<td></td>
<td>1 ½ cup</td>
</tr>
<tr>
<td>Meal</td>
<td>Food Type (e.g. wholegrain bread, vegemite)</td>
<td>Brand (e.g. Mias, Kraft)</td>
<td>Cooking method (or other comments)</td>
<td>Amount (in grams or mL or number of pieces)</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------------------</td>
<td>--------------------------</td>
<td>-----------------------------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>BREAKFAST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNCH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DINNER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNACKS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Obstetric data

**Obstetric history**

<table>
<thead>
<tr>
<th>Gravidity</th>
<th>Parity</th>
</tr>
</thead>
<tbody>
<tr>
<td>……………..</td>
<td>……………</td>
</tr>
</tbody>
</table>

Previous abortion: Nil / Spontaneous (n=……… ) /Induced (n=………)

Previous stillbirth (>20wks) Y / N GA at loss ……………
Previous pre-term birth Y / N GA at birth ……………

Reason for pre-term birth …………………………………………………………………………

Previous pre-eclampsia Y / N
Previous NND Y / N

EDD: ___ / ___ / ___
EDD based on: 1=Ultrasound / 2=LMP / 3=Both

Pre-pregnant weight ……………kg Height ……………cm
Wt at booking ……………kg GA ……………wks
Wt at delivery ……………kg GA ……………wks

**Antenatal information**

Rubella status: 1=Immune / 2=Not immune / 3=Unknown / 4=Equivocal

Hepatitis B status: 1=Positive / 2=Negative / 3=Unknown

Hepatitis C status: 1=Positive / 2=Negative / 3=Unknown

Anaemia in pregnancy Y / N
Hb at booking …………… GA ……………wks
Lowest Hb …………… GA ……………wks

Hypertension in pregnancy Y / N
Essential / chronic hypertension Y / N GA at onset ……………wks (pre-exist=0)
Gestational hypertension Y / N GA at onset ……………wks
Pre-eclampsia Y / N GA at onset ……………wks
Pre-eclampsia superimposed on chronic hypertension Y / N GA at onset ……………wks

Diabetes in pregnancy Y / N
Pre – existing Y / N Type I / Type II
Gestational diabetes Y / N GA at onset ……………wks
Insulin required Y / N GA at commencement ……………wks

Threatened abortion (< 20 wks) Y / N
No. of bleeds: …………… GA at bleed …………… / …………… / ……………wks
APH  
No. of bleeds: ……………  GA at bleed …………… / …………… / ………………wks
Reason:……………. (1=placenta prev 2=abruption 3=lower genital tract 4=post-coital 5=unknown)

**Premature rupture of membranes**  Y / N  GA …………….wks
Threatened preterm labour  Y / N  GA (first) ……………… wks
Tocolytics  Y / N  Drug used

GA …………… / …………… / ………………wks  Duration …………… / …………… / ………………hrs
Steroid therapy  Y / N  No. of doses ……………. (11.4mg)
Delivery after last dose : …………….(1=<24hrs 2=24-48hrs 3=48hrs-7days 4=>7days)

Chorioamnionitis  Y / N  Antibiotics  Y / N

**Hyperemesis** (requiring admission)  Y / N

**Asthma** during pregnancy  Y / N  Steroids required  Y / N

**Renal problems during pregnancy**  Y / N
Pre-existing  Y / N
Urinary tract infection  Y / N  no. of UTI ……………
Positive MSU  Y / N  organism

**Other** medical conditions  Y / N
Please specify……………………………………………………………………

**Surgery** during pregnancy  Y / N
Please specify……………………………………………………………………

**Antenatal EPDS** ……………… (score)  Date ___ / ___ / ___
Q4 + Q5 + Q6 = ………………… (score)
Mental health / psych problem  Y / N  Please
specify……………………………………………………………………

**Antenatal admissions**  Y / N
Total no. of admissions (<20wks) ……………  (>20wks)………
Total no. of days in hospital (<20wks) ……………  (>20wks)………

**Labour and delivery**
**Pre-term birth** (<37wks)  Y / N
Principal factor precipitating delivery:
<table>
<thead>
<tr>
<th>Condition</th>
<th>Y / N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous labour</td>
<td>Y / N</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Y / N</td>
</tr>
<tr>
<td>APH</td>
<td>Y / N</td>
</tr>
<tr>
<td>PROM</td>
<td>Y / N</td>
</tr>
<tr>
<td>IUGR</td>
<td>Y / N</td>
</tr>
<tr>
<td>Iso-immunization</td>
<td>Y / N</td>
</tr>
<tr>
<td>Elective</td>
<td>Y / N</td>
</tr>
</tbody>
</table>

Please specify …………………………………………………………………………

<table>
<thead>
<tr>
<th>Other</th>
<th>Y / N</th>
</tr>
</thead>
</table>

Please specify …………………………………………………………………………

**Onset of labour:**
- Spontaneous
- Induced
- Augmented
- No labour

<table>
<thead>
<tr>
<th>Cervical ripening</th>
<th>Y / N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGE2 Gel</td>
<td>Y / N</td>
</tr>
<tr>
<td>Foley’s catheter</td>
<td>Y / N</td>
</tr>
<tr>
<td>Other</td>
<td>Y / N</td>
</tr>
</tbody>
</table>

Please specify …………………………………………………………………………

**Indication for induction**
- Hypertension / pre-eclampsia | Y / N |
- Post dates                   | Y / N |
- Prelabour rupture membranes  | Y / N |
- IUGR                        | Y / N |
- Non-reassuring fetal well being (CTG) | Y / N |
- Diabetes                    | Y / N |
- APH                         | Y / N |
- Chorioamnionitis            | Y / N |
- Social                      | Y / N |
| Other                       | Y / N |

Please specify …………………………………………………………………………

**Syntocinon in labour**  | Y / N |

**Monitor in labour**  | Y / N |
- NAD                       | Y / N |
- Non-reassuring CTG        | Y / N |

Was delivery based on this result?  
- 1=Yes / 2=No / 3=Partially

**Scalp pH / lactate in labour**  | Y / N |
- Time  
  pH  
  pCO2  
  O2  
  ABE  
  lactate  
- Time  
  pH  
  pCO2  
  O2  
  ABE  
  lactate  

Was delivery based on this result?  
- 1=Yes / 2=No / 3=Partially
**Meconium** present 0=Nil / 1=Mec 1 / 2=Mec 2 / 3=Mec 3

**Fever** in labour (T°> 37.5) Y / N
- FBE done Y / N WCC
- Blood culture done Y / N
- Result…………………………
- MSU done Y / N Organism

**Duration** of labour
- First stage ………………hr
- Second stage ………………min
- Third stage ………………min

**Analgesia** in labour Y / N
- Nitrous oxide only Y / N
- IMI narcotic Y / N no. of doses ……………
- IVI narcotic Y / N no. of doses ……………
- Epidural Y / N
- Spinal Y / N
- Combined epid / spinal Y / N
- General anaesthetic Y / N
- Other Y / N

Please specify

**Other drugs in labour** Y / N
- Antiemetic Y / N
- Antibiotic Y / N Specify

**Antihypertensive** Y / N
- Other Y / N

Please specify

**Mode of delivery**
- SVD
- Assisted vaginal delivery
- Breech delivery
- Elective c/s
- Non-elective c/s

**Reason for assisted vaginal delivery**
- Delay
- Malposition
- Maternal exhaustion
- Avoid maternal effort
- Fetal distress
- Other
Please specify

Reason for Caesarean Section
Failure to progress / CPD
Fetal distress (incl. Non-reassuring fetal status)
Previous c/s
Breech presentation / malpresentation
Cord prolapse
Placenta previa
Severe hypertension / pre-eclampsia
Failed induction of labour
Multiple pregnancy
Other
Please specify

Perineum
Intact
First / second degree tear
Third degree tear
Episiotomy
Episiotomy & tear

Blood loss at delivery ........... ml

Placental weight ........... gm

Retained placenta Y / N
Action: ............. (1=MROP / 2=D&C / 3=Other)

Postnatal information
Secondary PPH Y / N
Action: ............ (1=D&C / 2=Antibiotics / 3=Other)
Sepsis requiring antibiotics Y / N
Cause: ............ (1=UTI / 2=Wound / 3=Perineum / 4=Mastitis / 5=Other / 6=Unknown)
Please specify

Other postnatal problem Y / N
Please specify

Date of discharge (mother): ___ / ___ / ___

Neonatal information

Date of delivery: ___ / ___ / ___
Time of delivery: ____ : ____ (24 hr)
Gestational age: ................. wks ............... days
<table>
<thead>
<tr>
<th>Stillborn</th>
<th>Y / N</th>
<th>Death / delivery interval .......... (days)</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td>Male / Female</td>
</tr>
<tr>
<td>Birthweight</td>
<td></td>
<td>............gm</td>
</tr>
<tr>
<td>Length</td>
<td></td>
<td>............cm</td>
</tr>
<tr>
<td>Head circumference</td>
<td></td>
<td>............cm</td>
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</table>

**Cord gases at delivery**

Arterial: pH ............. pCO2 ............. pO2 ............. ABE .............
Lactate .............

Venous: pH ............. pCO2 ............. pO2 ............. ABE .............

**Apgar score**

............. (1 min) ............. (5 min) ............. (10 min)

**TSR**

.............min

**Resuscitation**

Y / N

**Suction only**

Y / N

**O2**

Y / N

- Bag & mask: Y / N
- Intubation: Y / N
- Naloxone: Y / N
- Other: Y / N

Please specify...........................................................................

**Admitted to SCN**

Y / N (No if boarder)

Length of stay in SCN

............. days OR .............hrs

**Ventilation required**

Y / N

Duration

............. days OR .............hrs

**CPAP required**

Y / N

Duration

............. days OR .............hrs

**Oxygen required**

Y / N

Duration

............. days OR .............hrs

**Neonatal problems**

Y / N

- Jaundice requiring phototherapy: Y / N, Phototherapy: .............days
- Hypoglycaemia: Y / N (PGL < 2.5 mmol/l)
- Sepsis: Y / N

**TTN**

Y / N

**HMD**

Y / N

**Meconium aspiration**

Y / N

**Pnuemothorax**

Y / N

**Bronchopulmonary dysplasia**

Y / N

**PDA**

Y / N

**Intraventricular haemorrhage**

Y / N

**Seizures**

Y / N

**Weight loss > 10%**

Y / N

**Apnoea**

Y / N

**NEC**

Y / N

**Hypothermia**

Y / N

**Congenital anomaly**

Y / N

**Other**

Y / N

Please specify...........................................................................

187
Date of discharge:  ____ / ____ / ____

Discharged to:
Home with mother
PMH
Other

Please specify……………………………………………………………………………

Feeding at discharge
All breastfeeds
Breastfeed / EBM comps
Breastfeed / BMS comps
BMS
Other

Please specify……………………………………………………………………………

Neonatal death  Y / N
Age ..........days
Cause…………………………………………………………………………………
Appendix D

Exercise Training protocol & training sheets
### Weekly training progression protocol

<table>
<thead>
<tr>
<th>Phase (5-min blocks)</th>
<th>Program</th>
<th>Intensity (Target HR range, RPE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm up (WU)</td>
<td>Resistance Level 1 Pedal rate 50-60 RPM</td>
<td>55%–65% HR&lt;sub&gt;max&lt;/sub&gt;; RPE of 9-11</td>
</tr>
<tr>
<td>Continuous phase (CP)</td>
<td>Resistance Level 2 or 3 5 min continuous pedalling Pedal rate 60-80 RPM</td>
<td>65%–75% HR&lt;sub&gt;max&lt;/sub&gt;; RPE 12–12</td>
</tr>
<tr>
<td>Sprint phase (SP)</td>
<td>Resistance adjusted to maintain stability while sprinting; 15 s effort (Pedal rate &gt; 90 RPM) with 1 min 45 s active recovery</td>
<td>75%–85% HR&lt;sub&gt;max&lt;/sub&gt;; RPE 14–16</td>
</tr>
<tr>
<td>Hill Climb phase (HC)</td>
<td>Resistance Level 3 ++ 30 s hill climb effort (Pedal rate 60-70 RPM) with 1 min 30 s active recovery</td>
<td>75%–85% HR&lt;sub&gt;max&lt;/sub&gt;; RPE 14–16</td>
</tr>
<tr>
<td>Cool down (CD)</td>
<td>Resistance Level 1 Pedal rate 50-60 RPM</td>
<td>55-65% HR&lt;sub&gt;max&lt;/sub&gt;; RPE 9 – 11</td>
</tr>
<tr>
<td>Stretching</td>
<td>All major muscle groups</td>
<td>Gentle, static stretches held for 30 s</td>
</tr>
</tbody>
</table>

### Fortnightly progression chart

**Intervention week**  
*Beginner program for participants who are unaccustomed to exercise*

<table>
<thead>
<tr>
<th>Min</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
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<th>45</th>
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<tbody>
<tr>
<td>1-2</td>
<td>WU</td>
<td>CP</td>
<td>SP</td>
<td>HC</td>
<td>CD</td>
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<tr>
<td>3-4</td>
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<td>CP</td>
<td>SP</td>
<td>HC</td>
<td>CP</td>
<td>CD</td>
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<tr>
<td>4-5</td>
<td>WU</td>
<td>CP</td>
<td>SP</td>
<td>HC</td>
<td>SP</td>
<td>HC</td>
<td>CP</td>
<td>CD</td>
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<td>CP</td>
<td>HC</td>
<td>SP</td>
<td>CP</td>
<td>CD</td>
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<tr>
<td>9-10</td>
<td>WU</td>
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<td>SP</td>
<td>HC</td>
<td>SP</td>
<td>CP</td>
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<td>SP</td>
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<td>CP</td>
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<td>11-14</td>
<td>WU</td>
<td>CP</td>
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<td>SP</td>
<td>CP</td>
<td>HC</td>
<td>SPs</td>
<td>HC</td>
<td>CP</td>
<td>CP</td>
<td>CD</td>
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</table>
Training session records

Name: ........................................ Intervention week: .........................

Date: .......................  Fetal movement: Y / N  Session of week (please circle): 1  2  3

<table>
<thead>
<tr>
<th>Pre</th>
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</table>

Average HR: ..........  Max HR: ..........  Average RPE: ........ Distance: ..........  Duration: .....  

Comments:

Date: .......................  Fetal movement: Y / N  Session of week (please circle): 1  2  3

<table>
<thead>
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<th>Pre</th>
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<tr>
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</tbody>
</table>

Average HR: ..........  Max HR: ..........  Average RPE: ........ Distance: ..........  Duration: .....  

Comments:

Date: .......................  Fetal movement: Y / N  Session of week (please circle): 1  2  3

<table>
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<tr>
<th>Pre</th>
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</tr>
</tbody>
</table>

Average HR: ..........  Max HR: ..........  Average RPE: ........ Distance: ..........  Duration: .....  

Comments:
Rate of Perceived Exertion Scale (RPE Scale, Borg, 1982)

6  No exertion at all
7
8  Extremely light
9
10
11 Light
12
13 Somewhat hard
14
15 Hard (heavy)
16
17 Very hard
18
19 Extremely hard
20 Maximal exertion
Executive Summary

Objective

Gestational diabetes mellitus (GDM) is a common medical complication of pregnancy, placing the mother and her child at great risk of many serious acute and long-term health problems. Although regular exercise offers numerous benefits, its effectiveness in preventing GDM remains to be established. The Cycle Study is a research study that aims to determine whether a structured exercise training program (in addition to routine antenatal care) can prevent the recurrence of GDM (i.e. in women with a prior history of the condition). Within the program, relevant participants will be allocated into either a control group (no exercise training) or an exercise group whereby they will receive exercise training from a qualified trainer (i.e. you) in the comfort of their own home.

As the trainer of these women, you are responsible for the safety and well-being of both mother and child. This resource aims to provide you with essential information and tools to ensure the standardisation and effectiveness of each session among all women.

The Exercise Intervention

The ladies who are allocated into the exercise group receive 14 weeks of a supervised, home-based, stationary cycling program (commencing at 14 weeks of gestation and ending 27 weeks of gestation). This program is made up of a mixture of steady speed cycling, as well as seated short sprints and hill climbs so that a moderate to vigorous intensity workout can be achieved (See Appendix A). The training sessions are conducted three times each week, for a duration of 25-60 minutes depending on the ladies cycling ability and fitness level. The ultimate aim is to get the women up to 60 minutes of cycling by the end of the 14 week intervention however, this is not compulsory. The sessions should be very much tailored to the abilities of each individual (i.e. some women may be able to achieve 60 minutes by the fourth week, others may only be able to complete 40 minutes by the end of the intervention period).

Important Assessments at the Start of Each Training Session

Always check with the mother if she has felt any fetal movement (in the last 2 hours) prior to the start of each session. Fetal movements are typically felt from 18 weeks of gestation onwards. Secondly, blood
pressure and resting heart rate must be recorded prior to each session. The testing and training coordinator must be informed of any women presenting with a resting blood pressure higher than 140/90 mmHg.

Key Indicators to Look Out for to Avoid Over-Exertion during a Training Session

Be aware of the key indicators during each training session to ensure the safety of mother and child:
- Sudden paleness of the face
- Sudden swelling in limbs/face
- Dizziness/Headaches
- Shortness of breath that does not recover with rest
- Lack of hydration
- Complaints of chest pain/discomfort

Compulsory Components of Each Session

As with any exercise program, there should always be 5-10 min of warm up and cool down, followed by gentle stretches (See Appendix B).

Operational Procedures

Recruitment & Organising Initial Appointment

All sources of potential recruits will contact the Research Midwife regarding interest in the study. The Research Midwife will contact potential recruits by phone to explain the study in more detail and to determine whether they are indeed eligible to participate.

For women who are eligible and interested, the Research Midwife will obtain contact details and post out a Study Brochure, Information Sheet (including a map of where to come to SSEH at UWA) and a cover letter with some brief details (i.e. where to come / reimbursement of travel costs etc.)

The Research Midwife will then alert the Testing and Training Coordinator of a new participant, and email the participant’s contact details through. The Testing & Training Coordinator will contact the participant and arrange a time for baseline testing at UWA.
If the participant is assigned to the exercise intervention at the baseline testing session, the Testing &
Training Coordinator will put together the training paperwork (i.e. training sheets, map with directions to
the participant’s house and a cover sheet with participant contact details) and assign the participant a
trainer. NOTE: All training paperwork is kept in the Testing and Training Coordinator’s pigeon hole.
Once all the exercise sessions are completed, Exercise Physiologist must return all session record sheets
to the Testing & Training Coordinator.

Bike Delivery
The Testing & Training Coordinator will make the appointment with the participant on the day of testing.
The Testing & Training Coordinator may accompany the assigned trainer to deliver the exercise bike to
the participant for their first session. However, if the Testing and Training Coordinator is unavailable, the
trainer may need to deliver the bike and introduce themselves at this initial session. If this is the case, the
participant will be well informed that someone else (other than the person they have already met) will be
coming out to their house.
Ensure that you have the participant’s training paperwork before leaving for the first session.
Locate the exercise bike in an area with ample ventilation and access to at least 2 power points (one for
the bike and one for a fan).

Training Sessions
Cancellations should be made 24 hours in advance (applies to both parties).
Be punctual and ensure that you notify the participants if you are running late.
Check for any bike damage and tight any loose bolts before use.
Prior to starting exercise:
Check for fetal movement
Take Blood Pressure (Sitting)
Take Resting Heart Rate (Sitting)
Confirm the next appointment before leaving.
Check that you have packed away all equipment before leaving for your next appointment.
You may be asked to collect food diaries and accelerometers from the ladies (these are items that they will have from their initial appointment at SSEH) and if is the case, simply place them in the pigeon hole after collection.

Bike Collection

Ensure that you are aware of when your participant’s last training session is so that you can take the necessary steps (i.e. take Van 0) to collect and return the stationary bike to SSEH.

Offload the bike at SSEH for storage unless otherwise informed (i.e. it may need to be taken to another woman straight away and if this is the case, it does not need to be offloaded).

If the bike cannot be collected on the participant’s last session, inform the Testing and Training Coordinator who will organize another time for the bike to be collected (either by herself or the trainer).

The bike must be wiped down with sanitizer before delivery to the next participant.

Standardising the Program between Women

As the supervising trainer, your sessions should follow these basic guidelines: 1) a period of warm up, 2) main workout (broken down into steady speed, hill climbs and short sprints), 3) cool down and 4) stretching. However, use your creativity within each 5-min cycling block (i.e. the hill climbs, short sprints and steady speed cycling).

A definition of each cycling block is as follows:

Hill Climb

Bike resistance is increased to a point when the participant’s legs start to slow down and they are experience a weight pushing up against their feet.

Work zone should not be more that 1.5 min (i.e. participants must have a rest after every 1.5 min).

RPE should not exceed Hard (15-16) during this work zone.

Short Sprint

Ensure that enough resistant is applied to avoid participant bouncing on the seat during a sprint.

Sprints must not be longer than 30 s.

There must be an equal or longer rest break after each sprint.

RPE should not exceed Hard (15-16) during this work zone.
Steady Speed (Milage)

Work zone should be more than 1 min but not longer than 2.5 min.

Participant should not be able to maintain a conversation during work zone.

RPE should been maintained at Moderately Hard to Somewhat Hard (12-13) during work zone.

Participants should be coached to breathe steadily throughout.

Rest will not need to be longer than 1 min in this variation if breathing is coached.

Ensure that each of the exercise components can be achieved without significant impact on the participant’s posture (i.e. they should remain seated at all times and be able to maintain a straight spine throughout). NOTE: Some of the participants may experience pressure and discomfort in their tailbone which gets worse as the duration of the cycling bout increases. If this is the case, you may like to get them off the bike for a quick walk or stretch at various time-points throughout the session.

Ensuring a safe and effective workout for our participants

Every woman is different and as their pregnancy progresses, their moods will change along with the changes in their body. You may have one day where your trainee is alert, motivated and ready to go; but on the next day she may be exhausted and resistant to your coaching.

Be understanding and empathetic but remind them that they will feel much better after exercising.

Be adaptive during your sessions and always have in mind an easier workout for the day (but still sticking to overall structure of the workout).

Two scenarios:

The determined and overly driven mum

Some women may take this opportunity to push themselves in hopes of losing weight. Please remind them that pregnancy is not a time for weight loss. Women under this category will keep pushing themselves even if they are not feeling well. Watch for paleness in the face and shortness of breath even after rest. Encourage more seated hill climbs and subtly provide more prolonged rest. Request that they
come off the bikes for intermittent stretches. Do not prescribe other modes of exercise during their training session.

The distracted and lethargic mum

Be aware that you will probably have a 2-year old circling you during your session and offering you half eaten biscuits. More often than not, the mother may be preoccupied with the safety of her child, rather than focusing on your coaching. Some may take this opportunity to slack off. At this point, your babysitter instincts need to kick you! Reassure the mother that you will be her hands if her child needs to be caught. Instruct the mother to continue with her exercise and make sure she does it to her best ability while you entertain the child. For lethargic mums, advise them to focus on one 5-min block at a time and after each block, encourage them profusely to complete another 5-min block.

When is it not safe to start exercising?

Lack of Fetal Movement

Ideally, each participant’s sessions will be spaced with one day of rest in between sessions. Once the participant has notified that she has experienced some fetal movement for the first time, it is very important that she feels the fetus move in between subsequent sessions. If at the start of the session, the participant advises that she has not felt her fetus move since the last session, contact the Research Supervisor, Kym Guelfi immediately and postpone the session until medical attention is received. Kindly inform Testing & Training Coordinator after alerting the Research Supervisor of the situation.

Tachycardia at Rest

If resting heart rate is persistently over 100 bpm, contact the Research Supervisor, Kym Guelfi immediately and postpone the session until medical attention is received. Kindly inform the Testing & Training Coordinator after alerting the Research Supervisor of the situation.

High Blood Pressure at Rest
If resting blood pressure measures are equal or more than 140mmHg/100mmHg on two consecutive takes, contact the Research Supervisor, Kym Guelfi immediately and postpone the session until medical attention is received. Kindly inform the Testing & Training Coordinator after alerting the Research Supervisor of the situation.
Appendix F

Chapter 3 Study procedures
# Operational Procedure

## Logistics and Testing

<table>
<thead>
<tr>
<th>Date</th>
<th>Details</th>
<th>Author</th>
</tr>
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<tbody>
<tr>
<td>24 September 2012</td>
<td>Addition of EPDS</td>
<td>MJ Ong</td>
</tr>
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<td>Document Created: June 2011</td>
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<td>Last revised: April 2013</td>
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<td>Next revision due: Procedure</td>
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<tr>
<td>20 April 2013</td>
<td>Change of EPDS cutoff</td>
<td>MJ Ong</td>
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</table>
**Recruitment & Organising Initial Appointment**

- All sources of potential recruits will contact Cherry regarding interest in the study.
- Cherry will contact potential recruits by phone to explain the study in more detail and determine if they are eligible to participate.
- Eligible participants will be mailed a study brochure and Information Sheet (including map of where to come to SSEH at UWA; Appendix I & II) and a cover letter with some brief details (i.e. where to come / reimbursement of travel costs etc)
- Cherry then emails the screening form (see appendix III) to MJ.
- MJ then contacts participant and arrange a time for baseline testing at UWA.
- Gestation of recruits range between 7 weeks to 13 weeks of pregnancy.
- Once initial assessment is complete, MJ emails Cherry details of participant’s study number, randomised group, blood test appointment and Doctor’s details (see appendix IV).

**Special situations**
The eligibility of some potential participants may be discussed at some occasions. Some women would describe the current activity levels as regular; therefore, we need to find out in detail what they do, the frequency and how long they have been doing it. For example, if a woman says she walks 2-3 times a week, we would still include her in the study because the intensity of her walk most likely does not match up to the intensity achieved with the Cycle Study workout. However, if the woman is a serious gym goer that does Body Pump three times a week, she will be ineligible. When uncertainty, please consult Asst/Professor Kym Guelfi.

**Health & Fitness Testing at UWA School of Sport Science Exercise & Health**

**Bookings**

1. Check Alan Morton Lab and Gait Lab preparation room for availability before making appointment with participant.
   a. Alan Morton Lab – check Honour Room Computers or Ex Phy PhD Room
      i. To book, email don.gordon@uwa.edu.au and specify the equipment required.
      ii. Always use BLUE Metacart, FA04 Bike and Cyclemax computer (if possible)
   b. Gait Lab Preparation room
      i. Go to: http://aus.calendars.net/gaitlab
      ii. To book: click on the desired date and enter login details
      iii. Username: Gaitlab Password: Bookings
      iv. Click on Create and fill in the details accordingly as screenshot below
      v. Ensure to specify the use of the small prep room only and confirm your booking.
2. Ideally participants are booked in for baseline testing early in their 13-week of pregnancy. The participant must be booked in between 13 weeks and 14 weeks otherwise she will be deemed ineligible. The cut off for intervention to begin is **15 weeks of gestation**.

**Preparation: Data Sheets and Testing Equipment**

1. Each participant is allocated a Manila folder labelled with their study number and full name – contents should include:
   a. Participant Checklist – glued onto the front of the folder
   b. 13 week testing sheet (pink form)
   c. 28 week testing sheet (blue form)
   d. 2 sets of 5 questionnaires labelled #1XXX (13week) and #1XXXP (28week)
   e. 2 Pathwest blood forms
   f. 2 sets of 7-day food diary records

2. Copies of the data collection sheets and questionnaires are found in the Data Sheet File (white). Manila folders can be obtained from ladies at the Reception.

3. Once testing is complete, all forms should be returned to the participants manila folder and placed under lock and key.

4. All the equipment required for testing is located in the Testing box – contents include:
   a. Skinfold Caliper box – includes calipers and metal tape measure
   b. Heart Rate Monitor and strap
   c. Stethoscope
   d. Pink Clip Board for info sheet, data collection sheets & spare consent forms
   e. Petty Cash Receipt Book and UWA SSEH envelopes
   f. Cycle Study Laptop
   g. Activated Accelerometer & Cable

5. **Accelerometer Instructions:**

   **BEFORE USE**
   - Charge unit
   - Select “Initialize Device”
     - Don’t update firmware
     - Select “activity” and “step count”
     - 60 second EPOCH / normal filter
     - Set start and end date/time of data collection
     - Enter Subject Info for saving (i.e. 1001KGuelfi PRE or 1001KGuelfiPOST)

   **INSTRUCTIONS FOR USE / WEARING**
   - Device should be worn at the right hip (at the iliac crest) under clothing for all waking hours (MUST BE CORRECT SIDE UP!)
• Wear the belt snugly and to check the monitor placement regularly.
• Complete daily wear log and note when removing accelerometer for longer than 1 h to swim, shower, or nap.

AFTER USE
• Connect unit to study laptop
• Double click on Actigraph icon
• Select “Download Data”
  o Save ‘dat’ file in a known location with subject info (i.e. KGuelfi1001PRE)
• In “Analyse data” complete the following (selecting the relevant ‘dat’ file each time
  o Check graphically preview ‘dat’ file to check it worked
  o Create graphs (click to run day by day plot)
  o Create caloric output – use ‘combination’ (need subjects body mass)

6. Travel Reimbursement is in the BLACK cash box and should be placed under lock and key at all times. At each testing, place one $50 note into the UWA SSEH envelopes found with the Petty Case Receipt Book.

During the Testing Session
1. Prior to the session, obtain a temporary parking permit from the ladies at Reception. This permit can only be used within UWA Carparks (Staff & Paid Parking) and not City of Subiaco parking bays. Margaret will ask for participant’s name and date of testing.
2. Receive the participants at the carpark and welcome them to the Gait Lab Prep Room.
3. Explain the study to participant again and promote the FREE assessment and additional blood test they will be receiving with their involvement.
4. Reiterate the 50:50 chance of being assigned into either groups and explain that in order to do a comparison between routine antenatal care and effects of adding an exercise program, there needs to be two groups of women but BOTH GROUPS ARE Equally Important.
5. Explain that randomisation is carried out by the computer, stratified by BMI and maternal age.
6. Proceed by explaining what the session involves:
   a. Filling out the Participant Details form – especially partner and doctor’s details
   b. Answering the five questionnaires which takes 15-20 min, reminding them not to skip any questions and it should relate to how they feel at the current stage of pregnancy
   c. Anthropometric measurements will be done in this room
   d. Weight measurement and Tri-level bike test will be done in the lab upstairs
   e. Return to the room to receive an explanation for the 7-day food diary, accelerometer, and blood form.
   f. Randomisation at the end and issue travel reimbursement and receipt.
   g. Organise appointment for bike delivery and pick up of food diary and accelerometer for both groups of participants.
Note
If the Gait lab is not available, this session can be conducted entirely in the Alan Morton Lab. If the participant is bringing in their children, it is usually more convenient to use the Alan Morton Lab.

Important points to note

Questionnaires - Leave the room when participant is filling out the forms, in the meantime, the meta cart can be calibrated.

Tri-Level Fitness Test – reassure them that the test is submaximal and only exercise them to 75% of HRmax. This test is safe for mother and fetus and usually last 5-6min. Explain the process of the test and remind them that the first stage is very light pedalling. When calculating age-predicted HR, ensure that the same age is used in the calculation at pre- and post-testing even if participants has a birthday during the intervention period.

Pathwest Blood Forms - explain that they are found to be diabetic at 14 weeks, they will be withdrawn from the study. But in light of that, at least they find out about their condition early in their pregnancy rather than at 28 weeks. Stress on the fact it must be done in the next few days to ensure that we can promptly identity any underlying condition that requires medical attention and in the event they are assigned to the exercise group, intervention can begin promptly. Bring to their attention that our test includes addition time points so they will be receiving more needles that usual but that our test includes lipid analysis which is not usually included in routine antenatal care.

Follow Up – inform the participant you will be seeing them after 7 days to pick up the food diary and accelerometer. You will be calling them in two days to ask for the blood test appointment and to answer any questions they might have regarding the food diary and accelerometer. The delivery will be confirmed once we obtain their blood results.

After the testing session

Exercise Intervention Group: 14-Week Exercise Program
Control Group: 14 Weeks of usual activity

Data Entry

Data should be entered into the Cycle Study laptop as soon as possible to avoid a backlog. All questionnaires are to be entered with attention to detail.

Edinburg Postnatal Depression Scale (EPDS)
Special attention is to be given to the EPDS during data entry. Should a participant score 12 or more on this questionnaire, the following steps must be taken by the Testing and Training Coordinator.

1. Inform the Research Midwife of the participant. The Research Midwife will then:
a. contact the participant,
b. ask about participant’s circumstances and feelings in the last 7 days,
c. ask for more details about the circumstances (i.e. participant may have had a ‘good’ reason for feeling poorly - such as a car accident),
   - if the score is elevated that warrants further investigation - she will enquire if the participant is currently receiving care from any mental health professional(s) - if so this is the best referral and it is important to find out when (and if) the participant will be seeing this health professional again
   - if the participant is not seeing a health professional, the research midwife will arrange for a referral - to either her GP or her obstetrician providing antenatal care, or KEMH Psychological medicine or Rafael Centre. The choice of the actual referral will depend on what is the most appropriate. In many circumstances, she will be able to ask the participant for her preference. If no preferences - then most likely the main provider of the participant’s obstetric care will be notified.
d. The Research Midwife will follow up with a phone call after a few days.
e. Testing and Training Coordinator may ensure that the follow up is conducted with a reminder email to the Research Midwife.

### Blood Test

1. MJ will issue the Path West Forms to the participant during the initial assessment.
2. Two days later, MJ will ring the ladies and confirm that they have booked in for the 14 week test.
3. MJ will email the details to Cherry so that she can follow up with the results.
4. Cherry will inform MJ if a participant in the intervention group is diabetic. If so, bike delivery will be cancelled and participant becomes ineligible for the study.
5. Cherry receives the blood results for John to sign off.
6. Cherry sends a copy of the results to the participant’s GP/Doctor.
7. Cherry emails a copy to MJ for data entry
8. In the 22 weeks, MJ will mail the 28 week form to the participants with a letter (See Appendix V and repeats the process from step 2. The reason why the forms is sent out at 22 weeks of pregnancy is because some doctors will request that their participants go for the GTT at 26 weeks of pregnancy because they are an “at-risk” group. GTT can be done between 26-28 weeks of pregnancy.

### Bike Delivery & Preparation (after blood test results have been cleared)

1. MJ will make the appointment with the participant on the day of testing.
2. The assigned Exercise Physiologist is responsible for delivering the exercise bike to the participant.
3. Ensure that the driving directions are mapped out on Google Map before leaving for the first session.
4. Locate the exercise bike in an area with ample ventilation and access to at least 2 power points (one for the bike and one for the fan in summer)
5. Print out “Participant Info for Trainers” (Appendix VI) and 14 copies of the Training sheets (Appendix VII). These sheets plus the driving directions are placed in a clear plastic sleeve and passed on the assigned trainer.
## Training Sessions – Refer to Trainer Resource for more information

1. Cancellations should be made 24 hours in advance (applies to both parties)
2. Be punctual and ensure that you notify the participants if you are running late.
3. Check for any bike damage and tighten any loose bolts before use.

Prior to starting exercise:
- Take Blood Pressure (Sitting)
- Take Resting Heart Rate (Sitting)
- Assess RPE
- Confirm the next appointment before leaving
- Check that you have packed away all equipment before leaving for your next appointment.

## Bike Collection

1. MJ will inform Exercise Physiologist when the last training session is for a participant.
2. The bike will be collected at the last session (last day of 27-week of pregnancy)
3. The bike must be wiped down with sanitizer before delivery to the next participant.

## Participant Health and Fitness Reports

**13-week health and fitness assessment (See Report I)**
Report I is written to provide only limited information to avoid the Hawthorn Effect. This report is more so that the CONTROL subjects feel that they are getting something out of being in this study.

**28-week health and fitness assessment (See Report II)**

End of document
**What happens from here?**

<table>
<thead>
<tr>
<th>Next 7 days</th>
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<tbody>
<tr>
<td>1. Call the PathWest clinic closest to your home and book in for your</td>
<td>OGTT - Send a text to 0457 123 442 with your name and appointment</td>
</tr>
<tr>
<td>2. Complete the three sleep questionnaires.</td>
<td>date.</td>
</tr>
<tr>
<td>3. Complete the 7-day food diary in as much detail as possible.</td>
<td></td>
</tr>
<tr>
<td>4. Wear the red device firmly on your right hip at all times - Except when</td>
<td></td>
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<tr>
<td>in the shower, at the pool or beach, or when you are sleeping at night.</td>
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<table>
<thead>
<tr>
<th>After the 7th day</th>
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<tbody>
<tr>
<td>A member of The Cycle Study team will text you to organise a time to</td>
<td></td>
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<tr>
<td>pick up the sleep questionnaires, food diary and red device. If you will</td>
<td></td>
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<tr>
<td>not be home at the time of collection, you can leave them in your</td>
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<td>letterbox.</td>
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<tr>
<th>In the following weeks</th>
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<tr>
<td>Simply continue with your normal daily routine and attend your usual</td>
<td>antenatal appointments.</td>
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<tr>
<th>22 weeks</th>
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<tbody>
<tr>
<td>You will receive a letter from The Cycle Study informing you that your</td>
<td>28wk OGTT will be due in 4-6 weeks. A PathWest referral form will also</td>
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<tr>
<td>28wk OGTT will be due in 4-6 weeks.</td>
<td>be enclosed.</td>
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<td>If your doctor wants other blood tests done (e.g. Iron, Vitamin D) at the</td>
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<tr>
<td>same time as the OGTT, they must fill out a separate referral form. If they</td>
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<td>use referral forms for another pathology clinic (i.e. Clinipath, Western</td>
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<tr>
<td>Diagnostics, SJOG, etc.), please call the Testing and Training</td>
<td></td>
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<tr>
<td>Coordinator on 0457 123 442 to let us know. We are usually able to</td>
<td></td>
</tr>
<tr>
<td>organise it so that everything can be done in one visit at PathWest.</td>
<td></td>
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<tr>
<td>In the event that your doctor wants you to do this test earlier (e.g. ~26</td>
<td></td>
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<tr>
<td>wks of your pregnancy), that is ok as long as you inform us of your blood</td>
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<tr>
<td>test date so that we can obtain the results and forward them on to your</td>
<td></td>
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<tr>
<td>doctor.</td>
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<tr>
<th>26-27 weeks</th>
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<tbody>
<tr>
<td>You will receive a phone call from the Testing and Training Coordinator</td>
<td>to book you in for your 28-week health and Fitness Assessment at the</td>
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<tr>
<td>to book you in for your 28-week health and Fitness Assessment at the</td>
<td>UWA School of Sports Science, Exercise and Health. It will be a repeat</td>
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<tr>
<td>UWA School of Sports Science, Exercise and Health.</td>
<td>of the measurements you had when you were 13 weeks pregnant.</td>
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<tr>
<th>28 weeks</th>
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<tbody>
<tr>
<td>Attend your second Health and Fitness Assessment at the UWA School of</td>
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<td>Sports Science Exercise and Health.</td>
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**Finally, an analysis of your results will be completed and a report will be sent to you in the mail.**
What happens from here?

### Next 7 days
1. Call the PathWest clinic closest to your home and book in for your OGGT - Send a text to 0457 123 442 with your name and appointment date.
2. Complete the three sleep questionnaires.
3. Complete the 7-day food diary in as much detail as possible.
4. Wear the red device firmly on your right hip at all times - Except when in the shower, at the pool or beach, or when you are sleeping at night.

### After the 7th day
An Exercise Physiologist from The Cycle Study team will deliver an exercise bike to your home and will complete your first exercise session (~30 mins). The sleep questionnaires, food diary and red device will also be picked up.

### In the following weeks
An Exercise Physiologist from The Cycle Study Team will be visiting you three times a week to supervise your exercise sessions.

The exercise sessions are tailored to you however, we aim for each participant to progress up to 60 minutes (usually in 5-10 minute increments) three times a week over the 14 week intervention period. While this is the ideal scenario, we are aware that sometimes with pregnancy, possible illnesses and holidays, you may not end up reaching 60 minutes that is ok.

These sessions are designed to enhance your pregnancy and should not cause you to be out of energy by the end of the day. If you find that you are not recovering from the exercise sessions, or are finding them too stressful, please discuss this with your supervising Exercise Physiologist. Together, you can review the intensity of the sessions and come up with a more comfortable workout.

### 22 weeks
You will receive a letter from The Cycle Study informing you that your 28wk OGGT will be due in 4-6 weeks. A PathWest referral form will also be enclosed.

If your doctor wants other blood tests done (e.g. Iron, Vitamin D) at the same time as the OGGT, they must fill out a separate referral form. If they use referral forms for another pathology clinic (i.e. Clinipath, Western Diagnostics, SJOG, etc.), please call the Testing and Training Coordinator on 0457 123 442 to let us know. We are usually able to organise it so that everything can be done in one visit at PathWest.

In the event that your doctor wants you to do this test earlier (e.g. ~26 wks of your pregnancy), that is ok as long as you inform us of your blood test date so that we can obtain the results and forward them on to your doctor.

### 26-27 weeks
You will receive a phone call from the Testing and Training Coordinator to book you in for your 28-week Health and Fitness Assessment at the UWA School of Sports Science, Exercise and Health. It will be a repeat of the measurements you had when you were 13-weeks pregnant.

### 28 weeks
Attend your second Health and Fitness Assessment at the UWA School of Sports Science Exercise and Health.

### Next 7 days
1. Complete the three sleep questionnaires.
2. Complete the 7-day food diary in as much detail as possible.
3. Wear the red device firmly on your right hip at all times - Except when in the shower, at the pool or beach or when you are sleeping at night.

### After the 7th day
A member of the Cycle Study team will text you to organise a time to pick up the sleep questionnaires, food diary and red device.

Finally, an analysis of your results will be completed and a report will be sent to you in the mail.
End of thesis