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Exercise Guidelines for Women with Gestational Diabetes

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1. Introduction

1.1 Obesity and type 2 diabetes prevalence are increasing among women of child-bearing age

There has been a significant increase over the past few decades in the the prevalence of women of child-bearing age who are overweight (body mass index, BMI ≥ 25 kg/m^2) or obese (BMI ≥ 30 kg/m^2). Women of childbearing age are at an increased risk for obesity (Villamor & Cnattingius, 2006) and type 2 diabetes (Lipscombe & Hux, 2007) because of excessive weight gain during pregnancy and weight retention after delivery (Rooney et al., 2005). Data from the 2007-2008 "National Health and Nutrition Examination Survey" (NHANES) showed that 60% and 34% of American women aged 20-39 years were overweight or obese, respectively (Flegal et al., 2010). Abdominal obesity (i.e. waist circumference ≥ 88 cm; (Lean et al., 1995)), a risk factor for many chronic diseases (Després, 2001) also increased and reached 51.3% in 2007-2008 (Ford et al., 2010). Data from the "Pregnancy Risk Assessment Monitoring System" in nine states indicated that pre-pregnancy obesity increased from 13% to 22% between 1993 and 2002 (Kim et al., 2007). Worldwide population estimates of pre-pregnancy overweight is approximately 34% (Callaway et al., 2006; LaCoursiere et al., 2005) and that of pre-pregnancy obesity is 25% (Chu et al., 2009), which may be an underestimation. This escalating problem may contribute to the obesity and diabetes epidemics, as overweight women who gain 10% or more of their pre-pregnancy body mass are at higher risk for complications such as gestational diabetes mellitus (GDM; (Carducci et al., 1999)) and pregnancy-induced hypertension (Pole & Dodds, 1999). Additionally, higher recurrence of GDM has been associated with greater pre-pregnancy weight, BMI and excessive pregnancy weight gain (Foster-Powell & Cheung, 1998).

1.2 Women of child-bearing age are inactive, particularly overweight and obese women

Low levels of physical activity may be contributing to the obesity and type 2 diabetes epidemics in women of child-bearing age. Physical activity levels may be evaluated using different tools but pedometers and accelerometers provide an accurate and objective method of measuring walking and other ambulatory activities. Physical activity levels based on step counts have been defined: <5,000 steps per day = sedentary, 5,000-7,499 steps per day = low active, 7,500-9,999 steps per day = somewhat active, 10,000-12,499 = active and ≥

12,500= highly active (Tudor-Locke et al., 2008). Pedometer data from the "American On the Move" study showed that women aged 18-39 years took approximately 5500 steps per day (Bassett et al., 2010). Similar results were found by Tudor-Locke et al. using accelerometer data from the 2005-2006 NHANES (Tudor-Locke et al., 2010). They reported that women took approximately 5,800 steps per day (Tudor-Locke et al., 2010). Interestingly, the authors also reported that normal weight women took more steps per day compared to overweight and obese women (6,486, 5,069 and 5,782, respectively). In Canada, accelerometer results from the 2007-2008 "Canadian Health Measures Survey" showed that women aged 20-39 years took nearly 9,000 steps per day. Again, obese women were less active compared to normal weight women. Noteworthy, studies conducted on populations that have a lower prevalence of overweight and obesity, like Japan and Australia, reported higher steps per day (Inoue et al., 2006; McCormack et al., 2003). Achievement of public health recommendation (i.e ≥ 30 minutes of moderate-to-vigorous physical activity per day, accumulated in bouts lasting at least 10 minutes, on at least 5 out of 7 days (Canadian Society for Exercise Physiology & ParticipACTION, 2010; WHO, 2010)) were also examined using accelerometers. Results showed that less than 5% of women of child-bearing age meet these recommendations (Colley et al., 2011; Troiano et al., 2008; Tudor-Locke et al., 2010). Taken together, these findings showed that women of child-bearing age are inactive and suggested that being sedentary, and the prevalence of physical inactivity, may be contributing to the obesity and diabetes epidemics.

1.3 Maternal obesity is associated with impaired glucose metabolism

Entering pregnancy overweight or obese are closely linked to numerous unfavourable pregnancy outcomes, such as the development of impaired glucose tolerance (IGT) or GDM (Catalano & Ehrenberg, 2006; Chu et al., 2007; Davies et al., 2010; Nelson et al., 2009). Women who are obese prior to pregnancy are more likely to develop IGT as compared to normal weight women (Saldana et al., 2006; Tovar et al., 2009). Similarly, the risk of developing GDM has been shown to increase with increasing BMI: overweight and obese women have 2.14 (95% CI 1.82-2.53) and 3.56 (95% CI 3.05-4.21) times the risk of developing GDM compared to normal weight women (Chu et al., 2007). GDM prevalence rates are 0.7% in normal weight, 2.3% in overweight, 4.8% in obese and 5.5% in extremely obese (BMI ≥ 35 kg/m^2) women (Kim et al., 2010). More than 70% of women with GDM have a BMI of 25 kg/m^2 or higher (Kim et al., 2010). Similarly, maternal abdominal adiposity in early pregnancy has been associated with a positive glucose challenge test (i.e. glucose levels ≥ 7.8 mmol/L) and an increased risk of GDM (Brisson et al., 2010; Martin et al., 2009).

1.4 Excessive gestational weight gain is associated with impaired glucose metabolism

Another risk factor for developing IGT and GDM is excessive gestational weight gain (GWG). A cohort study revealed a positive relationship between weight gain in excess of the Institute of Medicine (IOM) guidelines (IOM, 1990) and the development of IGT, although these findings were limited to Hispanic women with a pre-pregnancy BMI ≥ 35 kg/m^2 (Tovar et al., 2009). Saldana et al. found in the "Pregnancy, Infection and Nutrition" (PIN) cohort a two-fold increased risk of IGT among overweight women who gained excessive weight up to the end of the second trimester (Saldana et al., 2006). Data from the "Project Viva" showed similar findings, with women in the highest quartile of GWG (i.e. 12.9 kg to

29.1 kg) being at increased risk for IGT, compared to those women in the lowest quartile of GWG (i.e -9.4 kg to 7.9 kg), independent of pre-pregnancy BMI (Herring et al., 2009). Finally, Kieffer et al. showed an estimated 2% increase in risk of GDM associated with each pound of maternal weight gained after adjusting for pre-pregnancy BMI (Kieffer et al., 2001). Excessive GWG, especially during the first trimester of pregnancy, has been found to be associated with an increased risk of GDM (Hedderson et al., 2010; Morisset et al., 2011), suggesting that timing of excessive GWG may be important and may be related to different patterns of metabolic change affecting glucose metabolism regulation.

Data from the 2006 "Maternity Experiences Survey", conducted in Canada, showed that 52% of Canadian women gained more than the recommended weight in pregnancy (Lowell & Miller, 2010). Moreover, the survey showed that women with a higher pre-pregnancy BMI were more likely than normal weight and underweight women to gain more weight than recommended. Fifty-five percent of overweight and obese women gained more weight than recommended, compared with 41% of those who were in the normal range and 26% of those who were underweight (Lowell & Miller, 2010). Previous studies reported similar findings, that is, overweight and obese women are more likely to exceed their target weight gain (Caulfield et al., 1996; Tovar et al., 2009; Saldana et al., 2006; Stuebe et al., 2009). Avoidance of excessive GWG may therefore constitute an opportunity for the prevention of impaired glucose metabolism during pregnancy.

1.5 Insulin resistance, the link between overweight/obesity, excessive gestational weight gain and impaired glucose metabolism

The underlying mechanism linking pre-pregnancy overweight/obesity to IGT or GDM is insulin resistance, coupled with an inadequate insulin response due to pancreatic beta-cell dysfunction (Buchanan & Xiang, 2005). Althought overweight and obese women present a similar 50% decrease in insulin sensitivity over the period of gestation, they are more insulin resistant than normal weight women throughout pregnancy (Catalano, 2010). Positive correlations have been reported between maternal body weight, BMI, fat mass and insulin resistance (Ahlsson et al., 2010). Maternal fat mass explained 36% of the variation in insulin resistance, and insulin resistance accounted for 62% of the variation in glucose production (Ahlsson et al., 2010). Adipose tissue is an active organ that secretes numerous factors involved in the development of insulin resistance, such as free fatty acids, leptin, adiponectin, interleukin-6 (IL-6), plasminogen activator inhibitor-1 (PAI-1), tumor necrosis factor-α (TNF-α), resistin, retinol binding protein 4, visfatin, etc. (Rasouli & Kern, 2008). In obese non-pregnant individuals, adipose tissue releases increased amounts of these factors, except adiponectin, which may explain the link between obesity, insulin resistance and type 2 diabetes (Kahn et al., 2006). In pregnant women, it has been reported that mean levels of adiponectin declined, and PAI-1 increased as BMI increments increased (Lowe et al., 2010). Recent studies have focused on the role of adipokines during normal pregnancy and pregnancy complicated by GDM and showed that the pattern of change in maternal circulating adipokine levels may be involved in the pathophysiology of GDM (Briana & Malamitsi-Puchner, 2009).

Excessive GWG may also further enhance normal pregnancy-induced insulin resistance and be linked to impaired glucose metabolism. Maternal adipose tissue represents 30% of GWG (IOM, 1990) but the proportion of GWG attributed to adipose tissue is more important in early pregnancy (Hedderson et al., 2010). The timing of GWG seems to be important as early excessive GWG has been associated with GDM risk (Hedderson et al., 2010; Morisset et al., 2011). It is therefore possible that rapid GWG in early pregnancy results in an increased release of "diabetogenic" factors, exacerbating earlier pregnancy-induced insulin resistance and thereby leading to IGT or GDM in women having beta-cell defects.

In summary, an increased number of women of child-bearing age are overweight or obese and physically inactive and these women will likely start their pregnancy overweight or obese and sedentary. These factors have been associated with an increased risk for excessive GWG, a deterioration in insulin resistance beyond that induced by pregnancy and impaired glucose metabolism. Therefore, any intervention that helps to limit excessive gestational weight gain and attenuate pregnancy-induced insulin resistance may be successful in preventing impaired glucose metabolism.

2. Physical activity is part of a healthy pregnancy

A minimal amount of physical activity must be maintained to achieve health benefits during pregnancy. Physical inactivity and a sedentary lifestyle may put the mother and fetus at risk for disease through altered maternal pregnancy adaptations (Mottola 2008). In fact, women who were the most active before pregnancy (Chu et al. 2007) and throughout pregnancy (Dye et al. 1997), had the lowest prevelence of GDM. If GDM and IGT can be prevented, overall rates of obesity and type 2 diabetes, especially in at risk population groups may also be decreased.

2.1 Maternal physical activity is associated with reduced risk of impaired glucose metabolism

Pregnancy-induced insulin resistance develops at the skeletal muscle level (Buchanan & Xiang, 2005). Investigators have demonstrated that exercise increases the rate of glucose uptake into the skeletal muscle, a process that is regulated by the translocation of the glucose transport protein GLUT-4 (Goodyear & Kahn, 1998; Hayashi et al., 1997; Ryder et al., 2001). Regular exercise in non pregnant individuals results in numerous beneficial adaptations in skeletal muscle, including increases in GLUT-4 expression, which contributes to an increased responsiveness of muscle glucose uptake to insulin (i.e. increased muscle insulin sensitivity) (Goodyear & Kahn, 1998; Hayashi et al., 1997; Ryder et al., 2001). This may explain the observed link between level of physical activity and improvement in glucose homeostasis and insulin sensitivity (Goodyear & Kahn, 1998; Koivisto et al., 1986), and a risk reduction of 50% for type 2 diabetes mellitus (T2DM) in at risk individuals (Madden et al., 2008; Yates et al., 2007). These physiological and molecular mechanisms underlying the beneficial effects of exercise may also be present in pregnant women since successful reduction in the risk of developing IGT and GDM have been reported in women who were active either before and/or during pregnancy (Tobias et al., 2010).

In the "Nurse Health Study II", women in the highest quintile of physical activity before pregnancy, specifically vigorous activity, had a 20% risk reduction for the development of GDM compared with inactive women (Zhang et al., 2006). In women not performing vigorous activity, brisk walking was also significantly associated with a reduced risk. Similarly, physical activity before pregnancy, particularly vigorous activity, was associated with a 44% risk reduction of GDM and a 24% risk reduction of any antepartum IGT in women participating in "Project Viva" (Oken et al., 2006). Women who reported physical activity both before and during pregnancy presented a greater risk reduction in both GDM and IGT (51% and 30%, respectively) compared with women reporting no activities in both time periods (Oken et al., 2006). Dempsey et al. reported that women who participated in any physical activity during the year before getting pregnant experienced a 56% risk reduction in GDM compared with inactive women, but those who engaged in physical activity during both time periods experienced a 69% reduced risk (Dempsey et al., 2004b). It has also been shown that pre-gravid physical activity (vigorous activity) was associated with a reduced risk of IGT in pregnancy, an effect likely mediated by enhanced insulin sensitivity (Retnakaran et al., 2009).

Similar results were found when investigating the effect of physical activity during pregnancy. Dye et al. reported that exercise during pregnancy (i.e. 30 minutes of exercise once or more per week) was associated with reduced rates of GDM, but only among women with a pre-pregnancy BMI>33 kg/m^2 (Dye et al., 1997). A study including only Latina women showed that those in the lowest quartile of sports or exercise in mid-pregnancy had a two-fold increased risk of IGT as compared with women in the highest quartile (Gollenberg et al., 2010). Similar association was found with total sedentary behaviours (a composite score of TV watching, sitting at work and sport or exercise reverse scores) (Gollenberg et al., 2010). A case-control study reported that women who participated in any recreational physical activity during the first 20 weeks of pregnancy experienced a 48% reduction in GDM risk, as compared with inactive women (Dempsey et al., 2004a). It has also been shown that women who were previously inactive but became active during pregnancy had a 57% risk reduction in GDM compared to those who remained inactive (Liu et al., 2008). Finally, a prospective study reported that increased physical activity during pregnancy was associated with decreased fasting insulin concentrations (Liu et al., 2010), suggesting that being active during pregnancy may prevent impaired glucose metabolism through attenuation of pregnancy-induced insulin resistance.

2.2 Maternal physical activity is associated with preventing excessive gestational weight gain

Another mechanism through which physical activity may prevent impaired glucose metabolism is by limiting excessive GWG. Prospective data from the "Project Viva" showed that 30 minutes per day of walking, vigorous physical activity or total physical activity during pregnancy were inversely associated with the risk of excessive GWG (Stuebe et al., 2009). Similar findings were found by Olson et al. who found that decreased physical activity was associated with excessive GWG (Olson & Strawderman, 2003). Lifestyle intervention studies also showed successful results with respect to the prevention of excessive GWG. Two reports using meta-analyses of intervention trials showed that exercise programs, combined with or without nutrition counselling, helps to limit GWG (Streuling et al., 2010a; Streuling et al., 2010b). Interventions that combined exercise and dietary counseling were found to be more successful in limiting GWG, with an average reduction of GWG of 1.2 kg (p=0.01) found in the intervention groups compared to the control groups (Streuling et al., 2010b). Three studies found significant lower GWG in the exercise plus nutrition intervention group compared with the control groups (Asbee et al., 2009; Claesson et al., 2008; Shirazian et al., 2010), 3 studies found a non significant trend in lower GWG in the intervention group compared with the control group (Gray-Donald et al., 2000; Guelinckx et al., 2010; Olson et al., 2004) and three found no significant results (Hui et al., 2006; Kinnunen et al., 2007; Polley et al., 2002). Findings from intervention studies using only exercise were less consistent than findings from intervention studies combining exercise and nutrition. Seven trials reported a trend for less GWG in the exercise group (Barakat et al., 2009; Cavalcante et al., 2009; Clapp et al., 2000; Ong et al., 2009; Santos et al., 2005; Sedaghati et al., 2007; Yeo, 2009) which was significant in only one of these trials (Sedaghati et al., 2007). Five trials reported that women in the exercise group did not gain significantly less weight than women in the control group (Collings et al., 1983; Garshasbi & Faghih Zadeh, 2005; Hopkins et al., 2010; Marquez-Sterling et al., 2000; Prevedel et al., 2003). An average reduction in GWG of 0.6 kg (p=0.03) was found in the exercise intervention groups compared to the control groups (Streuling et al., 2010a). A single arm intervention study, combining exercise and diet, reported that 56% of obese women kept their GWG to ≤ 6 kg (study weight goal) and no cases of reduced glucose tolerance were observed (Lindholm et al., 2010). Finally, a recent study conducted in our laboratory showed that excessive GWG was prevented in 80% of overweight and obese women using a Nutrition and Exercise Lifestyle Intervention Program (NELIP) (Mottola et al., 2010).

In summary, the prevailing literature clearly indicates that physical activity before and/or during pregnancy has a protective effect against excessive GWG and impaired glucose metabolism. Results from intervention studies suggest that in order to be the most successful in limiting GWG, and thus in helping to prevent impaired glucose metabolism, lifestyle interventions should promote both regular physical activity and healthy eating habits. Promoting a healthy lifestyle during pregnancy, especially in overweight and obese women, becomes increasingly important in the context of the prevention of impaired glucose metabolism.

2.3 Guidelines for physical activity during pregnancy

Active promotion of physical activity for pregnant women is strongly recommended by professionnal societies, such as the American College of Obstetricians and Gynecologists (ACOG, 2002), the Royal College of Obstetricians and Gynaecologists (RCOG, 2006), the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Canadian Society of Exercise Physiologists (CSEP) (Davies et al., 2003). The ACOG suggested that "in the absence of either medical or obstetric contraindications, 30 minutes or more of moderate exercise a day on most, if not all, days of the week is recommended for pregnant women" (ACOG, 2002). The recent opinion statement from the SOGC (Davies et al., 2010) on obesity during pregnancy strongly suggests that regular exercise during pregnancy may help to reduce the risk of medical complications associated with maternal obesity. However, all pregnant women should be medically prescreened and consult their health care provider before engaging in an exercise program. In 2008, the Unites States government released physical activity guidelines for Americans, including recommendations specifically for pregnant women to attain at least 150 minutes of moderate intensity aerobic activity per week if not already highly active or doing vigorous intensity activity. Healthy pregnant women who engaged in vigorous aerobic activity or are highly active prior to pregnancy are encouraged to continue physical activity (U.S Department of Health and Human Services 2008). Finally, the joint SOGC/CSEP Clinical Practice Guidelines encourage women to exercise if they have no contraindications (Davies et al., 2003). The SOGC/CSEP Clinical Practice Guidelines provide detailed recommendations about the frequency, intensity, time and type of exercise, following the FITT principle for exercise prescription. Women should exercise 3 to 4 times per week, starting with 15 minutes of aerobic activity at a target heart rate intensity and increasing time slowly to a maximum of 30 minutes per exercise session. All aerobic activity should be preceded by 10- to 15-minutes of warm-up and followed by 10- to 15-minutes of cool-down. Appropriate exercise intensity may be monitored by using target heart-rate zones, the Borg-scale (rating of perceived exertion, RPE) or the "talk test" (Davies et al., 2003). Heart-rate zones that are provided in the guidelines correspond to moderate-intensity exercise (i.e. 60-80% of maximal aerobic capacity, $VO_{2\ max}$). Aerobic exercise in which large muscle groups are used, including walking, stationary cycling, aqua exercise, or low-impact aerobics are recommended for low risk pregnant women (Davies et al. 2003).

Overweight and obese women can participate in exercise, if they have no contraindications to being physically active. Twenty medically pre-screened obese and 20 normal weight pregnant women participated in a graded treadmill exercise test to volitional fatigue to examine the impact of obesity on the ventilatory response to weight-bearing exercise during pregnancy (Davenport et al., 2009). We concluded that exercise ventilatory response is increased during pregnancy but is not affected further by obesity during graded treadmill exercise (Davenport et al., 2009). This is important in that there is no apparent ventilatory limitation to submaximal weight-bearing exercise representing daily living activities such as walking, in pregnant obese women, which lends support to the feasibility of exercise prescription in this population group (Mottola, 2009). Target heart rate zones developed for normal weight pregnant women may be too difficult for overweight and obese women to obtain, and thus we developed and validated target heart rate zones for medically pre-screened overweight and obese women at a much lower intensity but high enough to achieve aerobic benefits (Davenport et al. 2008a). The intensity is approximately 20-39% heart rate reserve (HRR), and at a normal walking pace which may help with compliance in this population group.

Currently, there are no step recommendations for pregnant women but those that have been defined for adults (Tudor-Locke et al., 2008) may be used for pregnant women. As walking is the most reported activity during pregnancy (Evenson et al., 2004; Evenson & Wen, 2010; Mottola & Campbell, 2003; Petersen et al., 2005), providing step recommendations to pregnant women may encourage them to be more active. Previous studies conducted in our laboratory showed that pregnant women took more than 10,000 steps per day when a 40-minute walk was added to their usual daily activities (Davenport et al., 2008b; Mottola et al., 2010).

2.4 Are pregnant women meeting the physical activity guidelines?

Although maternal physical activity has clear health benefits on pregnancy outcomes, and professional societies strongly recommend active promotion of physical activity for pregnant women, most women remain inactive during pregnancy. In Canada, only 30% of pregnant women meet the adult step recommendations of 10,000 steps per day (Cohen et al., 2010). Data from large cohort studies, such as the "Behavioral Risk Factor Surveillance System" (BRFSS), NHANES and PIN showed that the majority of women do not meet the recommendations for physical activity during pregnancy, based on information collected by interviews or questionnaires (Borodulin et al., 2008; Evenson et al., 2004; Evenson & Wen, 2010; Petersen et al., 2005). The guidelines from the ACOG and from the Center for Controlled Disease (CDC)/American College of Sports Medicine (ACSM) both suggest 30 minutes or more of moderate-intensity activity on most of the days of the week, but differ on the type of activity, as guidelines for ACOG include only exercise and guidelines from CDC/ACSM include any type of physical activity. If the recommendations for physical activity were based on the ACOG guidelines, only 3% of pregnant women meet the recommendations (Borodulin et al., 2008). If the recommendations for physical activity were based on the CDC/ACSM guidelines, approximately 15% of pregnant women meet the recommendations (Borodulin et al., 2008; Evenson et al., 2004; Evenson & Wen, 2010; Petersen et al., 2005). In Spain, 20% of women comply with ACOG criteria whereas 70% comply with CDC/ACSM criteria (Amezcua-Prieto et al., 2010).

In summary, most women are physically inactive during pregnancy. This may be contributing to excessive GWG given that women who are meeting the recommendations for exercise during pregnancy are more likely to achieve appropriate GWG (Cohen et al., 2010). Moreover, given the clear association between physical inactivity during the perinatal period and risk for impaired glucose metabolism, physical inactivity may be contributing to the 10 to 100% increase in GDM prevalence observed in several race/ethnic groups during the past 20 years (Dabelea et al., 2005; Ferrara, 2007; Getahun et al., 2008).

3. Exercise as an adjunctive therapy for gestational diabetes mellitus management

3.1 Conventional management of gestational diabetes mellitus

The primary management for women with GDM is control of energy intake, usually referred to as medical nutrition therapy (MNT) (Metzger, 2006). As a dietary intervention, the goals of MNT are to provide adequate nutrition for the mother and fetus, provide sufficient calories for appropriate maternal weight gain, maintain normoglycemia, and avoid ketosis (Franz et al., 2002). The dietary plan suggested by a registered dietitian usually includes eating smaller meals more often, more choices of complex carbohydrates with a low glycemic index, and the elimination of high glycemic foods, including carbonated beverages, sweets, and cake (CDA, 2008). Self-capillary glucose monitoring using a glucometer may be recommended up to seven times per day. The goal of monitoring is to maintain glucose concentrations in acceptable ranges. The Canadian Diabetes Association (CDA) recommends maintaining the following capillary blood glucose values: pre-prandial glucose < 5.3 mmol/L, 1-hour post-prandial glucose < 7.8 mmol/L, and 2-hour post-prandial glucose < 6.7 mmol/L. The Fifth International Workshop-Conference on Gestational Diabetes Mellitus guidelines are the same (Metzger et al., 2007). If after 2 weeks of MNT, failure to control capillary glucose concentrations will progress to management of glycemia by insulin injections. It is imperative that maternal blood glucose be maintained below these values, either with MNT plus insulin injections or MNT and lifestyle changes. The type and amount of insulin injected is beyond the scope of this article but depends on medical intervention and management (Metzger et al., 2007).

3.2 Exercise/lifestyle management for women with gestational diabetes mellitus

Exercise has long been accepted as an adjunctive intervention in the management of diabetes in non pregnant individuals (ADA, 2011; CDA, 2008; Colberg et al., 2010). In type 2 diabetic individuals, exercise has been reported to improve insulin sensitivity and insulin-stimulated muscle glucose uptake (Kennedy et al., 1999), to have a positive effect on glycemic control and to decrease cardiovascular risk (Kavookjian et al., 2007). However, there is still controversy regarding the benefits of exercise in improving glycemic control in GDM women, despite endorsements by professionnal organisations. The ACOG (ACOG, 2001) suggests that "women with GDM who lead an active lifestyle should be encouraged to continue a program of exercise approved for pregnancy." The American Diabetes Association (ADA) (ADA, 2004) suggests that "women without medical or obstetrical contraindications be encouraged to start or continue a program of moderate exercise as part of treatment for GDM." The CDA (CDA, 2008) suggests that "physical activity should be encouraged, with the frequency, type, duration and intensity tailored to individual obstetric risk." The recommendation from the Fifth International Workshop-Conference on GDM suggests "planned physical activity of 30 minutes/day is recommended … Advising GDM patients to walk briskly or do arm exercises while seated in a chair for at least 10 minutes after each meal accomplishes this goal" (Metzger et al., 2007).

Evidence-based studies determining the frequency, intensity, time, and type of activity are needed to provide the best possible outcomes for women with GDM. When exercise was evaluated for controlling blood glucose concentrations or for delaying or preventing insulin therapy, the results were discordant. In the recent ACSM/ADA joint position statement, level of evidence concerning the effect of physical activity to control GDM was non-existent for the ADA, and weak for the ACSM (Colberg et al., 2010). These mixed results could be due to the non-randomization of the subject pool, the different anthropometric characteristics of the women, small sample sizes, lack of well-controlled or reported exercise intensity, the differences in exercise modalities, or questionable compliance to the exercise program. Consequently, because of lack of consistent evidence regarding the benefits of exercise in improving glycemic control in GDM women, exercise remains an adjunctive therapy.

The acute effect of exercise on glucose excursion has been evaluated by several authors (Table 1). Avery and Walker (2001) reported that a single 30-minute bout of exercise on a cycle ergometer at 35% or 55% of maximum oxygen consumption ($VO_{2\ max}$) improved glucose excursion compared with rest in women with GDM (Avery & Walker, 2001). Garcia-Patterson et al. found similar results, showing that light postprandial walking at 2.5 km/h decreased glucose excursion in GDM women (Garcia-Patterson et al., 2001). Lesser et al. (1996) determined the effects of a single bout of stationary cycling for 30 minutes at 60% $VO_{2\ max}$, comparing six GDM women to five normal glycemic pregnant women. The effects of a mixed meal 14 hours after the exercise bout were examined. In contrast to the above studies, no improvement in glucose excursion due to the exercise was found in the GDM women. This could be due to a mixed meal being used in the acute experiment and because measurements occurred 14 hours after the exercise bout.

The chronic effect of exercise for controlling blood glucose concentrations has also been investigated (Table 2). A 6-week arm ergometry exercise program was successful in normalizing fasted and 1-h plasma glucose concentrations and glycosylated hemoglobin (HbA1c) in GDM women randomized to diet therapy plus exercise compared with diet therapy alone (Jovanovic-Peterson et al., 1991). The exercise program consisted of 20 minutes of arm ergometry, three times per week, at an intensity less than or equal to 50% $VO_{2\ max}$. The results of this study gave rise to the recommendation of arm exercise for GDM women mentioned above. In contrast to the above studies, Bung et al. (Bung et al., 1991) randomized GDM women into a group with diet and insulin therapy or diet and exercise. The exercise program consisted of stationary cycle ergometry (50% $VO_{2\ max}$) for 45 minutes (three 15-minute bouts with two rests), three times per week. Because no differences in

References	Population	Intervention program	Gestational age	Main findings
(Lesser et al., 1996)	N=11: 6 GDM, 5 NGT Ethnicity: na Pre-pregnancy BMI (kg/m^2): NGT=24.3±0.9 GDM=25.9±1.8 Age (years): NGT=23.7±20 GDM=27.6±2.8	Control situation Standardized breakfast, followed by blood samples. Exercise situation Intensity: 60% $VO_{2\ max}$ Duration: 30 min Type: stationary cycle. Exercise performed 14 h before standardized breakfast, followed by blood samples.	28-38 w of gestation	Similar mean values for fasting glucose, peak glucose, area under the glycemic curve with vs without exercise. Similarly, plasma insulin levels did not differ between protocols for either group of subjects. Not successful
(Avery & Walker, 2001)	N=13, GDM Ethnicity: na Pre-pregnancy BMI (kg/m^2): 29.0±7.4 Age (years): 31.9±3.6	Control situation Remained seated for 2h30 Exercise situation Intensity: 35% and 55% $VO_{2\ max}$ Duration: 30 min Type: stationary cycle. The women exercised at the two intensities for 30 min and rested for 2 h after each session.	30-34 w of gestation	Blood glucose levels were significantly different after 30 min of rest, low- and moderate-intensity exercise: Rest: 5.2 mmol/L Low: 4.3mmol/L Mod: 3.9 mmol/L. Successful
(Garcia-Patterson et al., 2001)	N=20, GDM Ethnicity: na Pre-pregnancy BMI: na Age (years): 33.5±4.6	Control situation remained seated for 2h after a standard breakfast. Exercise situation walked self-paced (2.5 km/h) in the 1st hour after breakfast and remained seated during the 2nd hour.	30.7±5.5 w of gestation	During control situation, higher 1-h postprandial blood glucose (p=0.001) and 1-h blood glucose excursion (p=0.001) compared to exercise situaton. Successful

NGT – normal glycemia; BMI – body mass index.

Table 1. Summary of studies using acute exercise to change blood glucose concentrations in women with gestational diabetes mellitus (GDM).

glycemic control were found between groups, the authors suggested that exercise may provide avoidance of insulin therapy through an increase in insulin sensitivity. In another study, GDM women were randomized to a partial home-based exercise program (70% of estimated maximal heart rate) and compared with GDM women with no structured exercise program (Avery et al., 1997). Although the exercise program improved the cardiorespiratory fitness of the GDM women, glucose excursion was not different compared with the women with no structured exercise program (Avery et al., 1997). More recently, Artal et al. (2007) randomized obese GDM women into MNT plus exercise (60% $VO_{2\ max}$) or MNT alone. Results showed that the MNT plus exercise group limited GWG and had no adverse pregnancy outcomes. The authors concluded that placing obese women with GDM on a lifestyle intervention strategy of weight gain restriction may optimize pregnancy outcomes and impact future weight management behaviors. Using a different exercise modality, de Barros et al. (de Barros et al., 2010) randomized GDM women into a resistance exercise program (elastic band) group or MNT alone group. A reduction in the number of patients who required insulin was obseved in the exercise group compared with the MNT group. Furthermore, the percentage of time spent within the proposed target glucose range was higher in the exercise group compared with the MNT group.

In a 2004 retrospective chart review from London, Canada, assessing conventional management of women diagnosed with GDM, Davenport et al. (2005) showed that by 30 weeks of pregnancy, 62% of these women required insulin therapy (after trying conventional management for 2 weeks after diagnoses). Of this cohort, women with a pre-pregnancy BMI of 25 kg/m^2 or greater were 2.6 times more likely to require insulin therapy than those women with a BMI below 25 kg/m^2 . The average pre-pregnancy BMI of women requiring insulin therapy was 30.6 ± 6.4 kg/m^2. This high incidence of insulin therapy in women with a BMI of 25 kg/m^2 or greater may indicate the need for intensive therapy to delay or prevent insulin usage. In women with an early GDM diagnosis (at 16 to 20 weeks of gestation) who followed a structured walking program (30% HRR), 3–4 times per week in addition to conventional management, only 50% required insulin therapy (Davenport et al., 2005). In another study evaluating 30 GDM women, 10 following conventional management plus a low-intensity walking program (30% HRR, 3–4 times per week) matched by insulin useage to 20 women following conventional management alone, we reported lower mean capillary glucose concentrations at the end of pregnancy (fasting and 1h after meals) in the exercising group (Davenport et al., 2008b). The lower glucose concentrations were achieved while requiring fewer units of insulin per kg per day. Using a different exercise modality, Brankston et al. (Brankston et al., 2004) randomized GDM women to a group with diet alone or a group of diet plus circuit-type resistance training. The number of women requiring insulin was not different between groups. However, they found that within the diet plus exercise group, 30% of the women who exercised 2-3 times per week were prescribed insulin therapy compared to 67% of those who exercised <2 per week. Moreover, a subgroup analysis that examined only overweight and obese women showed a lower incidence of insulin use, a lower prescription of insulin and a longer delay from diagnosis to the initiation of insulin therapy in the diet plus exercise group.

Taken together, the above results are very encouraging. However, future lifestyle intervention programs are required to confirm these promising results and to determine the frequency, intensity, time, and type of activity that are needed to provide the best possible outcomes for women with GDM.

References	Study type	Population	Intervention program	Length of program	Main findings
(Jovanovic-Peterson et al., 1991)	Randomization: diet (D) vs diet+exercise (D+EX) group	N=19: D=9, D+EX=10 Ethnicity: na Pre-pregnancy BMI (kg/m^2): na Age (years): D=31.1±2.8 D+EX=29.5±2.5	Diet 24 to 30 kcal/kg/24 h; 40% CHO, 20% P, 40% F Exercise Freq: 3/week Intensity: 50% VO_2max Duration: 20 min Type: arm ergometry	6 weeks	Lower HbA1C, fasting and 1-hour plasma glucose concentrations in D+EX group compared to D group ($p<0.001$ for all). Successful
(Bung et al., 1991)	Randomization: diet+exercise (D+EX) vs diet+insulin (D+I) group	N=34: D+EX=17, D+I=17 Ethnicity: Hispanic Pre-pregnancy BMI (kg/m^2): na Age (years): D+EX=31.0±4.5 D+I=32.0±5.7	Diet 30 kcal/kg/day Exercise Freq: 3/week Intensity: 50% $VO2_{max}$ Duration: 45 min (3x15 min) Type: stationary cycle	From diagnosis (30±2 w of gestation) to delivery	No differences in glycemic control between D+EX and D+I groups. Similar maternal and neonatal outcomes between groups. Successful
(Avery et al., 1997)	Randomization: exercise (EX) vs control (CON) groups	N=29: EX=15, CON=14 Ethnicity: Caucasian Pre-pregnancy BMI (kg/m^2): EX=28.4±7.6 CON=25.5±5.5 Age (years): EX=32.2±4.9 CON=30.4±5.1	Exercise Freq: 3-4/week (2 supervised) Intensity: 70% (220-age) Duration: 30 min (including 5 min warm-up and cool-down) Type: stationary cycle or walking	From <34 w of gestation to delivery	No difference in HbA1C and insulin usage among EX and CON groups. Similar infant birth weight and incidence of hypoglycemia between groups. Not successful
(Brankston et al., 2004)	Randomization: diet (D) vs diet+exercise (D+EX) group	N=32: D=16, D+EX=16 Ethnicity: na, from Canada Pre-pregnancy BMI (kg/m^2): D=28.0±5.7 D+EX=25.9±3.4 Age (years): D=31.3±5.0 D+EX=30.5±4.4	Diet 40% CHO, 20% P, 40% F. 3 meals and 3 snacks. Exercise Freq: 3/week Intensity: <140bpm Type: Circuit-type resistance training.	From 26-32 w of gestation to delivery	Within D+EX group, 30% of the women who exercised 2-3 per week were prescribed insulin therapy compared to 67% of those who exercised <2 per week. In overweight women only, lower incidence of insulin use, lower prescription of insulin and longer delay from diagnosis to the initiation of insulin therapy in D+EX vs D group ($p<0.05$). Successful

References	Study type	Population	Intervention program	Length of program	Main findings
(Artal et al., 2007)	Self-enrollement in diet (D) vs diet+exercise (D+EX) groups	N=96: D=57, D+EX=39 Ethnicity: 55-60% caucasian from the US Pre-pregnancy BMI (kg/m²): ≥ 30 Age (years): D=30.6±5.5 D+EX=32.4±5.3	Diet CHO 40%–45% Exercise Freq: 1/week in lab, unsupervised ex. session at home Intensity: 60% $VO_{2\ peak}$ Duration: 20 min Type: treadmill or stationary cycle	<33 w of gestation until delivery	Lower GWG per week in D+EX group than in D group (0.1±0.4 kg vs 0.3±0.4 kg, p <0.05). Similar pregnancy outcomes between the groups. Successful
(Davenport et al., 2008b)	Exercise (EX) vs conventional management (CM) group -matched by BMI, insulin use -2 CM/EX	N=30: EX=10, CM=20 Ethnicity: na, from Canada Pre-pregnancy BMI (kg/m²): ≥ 25 Age (years): EX=33.4±3.3 CON=33.3±5.3	Exercise Freq: 3-4/week, Intensity: 30% HRR mild Duration: 25-40 min Type: treadmill	Minimum 6 weeks (from diagnosis to delivery)	Lower mean capillary glucose levels at the end of pregnancy (fasting and 1h after meals) in EX group but not in CM group (p <0.05). Ex group needed less insulin than CM group. Successful
(de Barros et al., 2010)	Randomization: exercise (EX) vs control (CON) group	N=64: EX=32, CON=32 Ethnicity: na, from Brasil Pre-pregnancy BMI (kg/m²): EX=25.34±4.16 CON=25.39±3.81 Age (years): EX=31.8±4.87 CON=32.40±5.40	Exercise Freq: 3/week (2 at home) Intensity: "somewhat heavy" exercise perception. Duration: 30-40 min Type: resistance training circuit (elastic band)	24-34 w of gestation to delivery	Reduction in the number of patients who required insulin in the EX (7/32) compared with the CON group (18/32) (p=0.005). The % of time spent within the proposed target glucose range was higher in EX group compared with CON group (p=0.006). Successful

BMI – body mass index; Freq – frequency; CHO – carbohydrate; P – protein; F – fat; na – not given; HRR – heart rate reserve.

Table 2. Summary of studies using the chronic effect of exercise to control blood glucose concentration, to delay or prevent insulin usage in women with gestational diabetes mellitus (GDM).

3.3 Exercise guidelines for women with gestational diabetes mellitus

In 2003, Artal proposed guidelines to develop exercise programs for pregnant women with GDM (Artal, 2003). He suggested 3 to 4 exercise sessions per week, at 50% $VO_{2\ max}$ for three

15-minute bouts with 5-minute rests between each, for a total of 45 minutes. The joint SOGC/CSEP Clinical Practice Guidelines (Davies et al., 2003) provides detailed recommendations regarding frequency, intensity, time, and type of activity for healthy pregnant women. The same recommendations may be used for pregnant women with GDM, except that the intensity of exercise might be adapted and that precaution should be taken, especially for women using insulin. The SOGC/CSEP Clinical Practice Guidelines provides heart-rate zones corresponding to exercise of moderate intensity (i.e. 60-80% of $VO_{2\ max}$). However, this intensity may be too high for pregnant women with GDM who are overweight or obese and possibly sedentary. The ACSM suggested that previously sedentary overweight and obese pregnant women should initiate an aerobic exercise program at an intensity equivalent to 20% to 39% of reserve aerobic capacity ($VO_{2\ reserve}$) (ACSM, 2005). These developed and validated target heart-rate zones based on age, equivalent to 20% to 39% $VO_{2\ reserve}$ are 102 to 124 beats per minute (bpm) for overweight and obese women 20 to 29 years of age and 101 to 120 bpm for those aged 30 to 39 years (Davenport et al., 2008a).

Interestingly, lower-intensity aerobic exercise seems to be more efficient in term of glycemic control than moderate-intensity exercise for pregnant women. Indeed, all intervention studies that used lower-intensity aerobic exercise (i.e. ≤60% $VO_{2\ max}$) were successful in controlling blood glucose concentrations and/or limiting/preventing insulin therapy (Artal et al., 2007; Bung et al., 1991; Davenport et al., 2008b; Jovanovic-Peterson et al., 1991) whereas the only study that used moderate-intensity aerobic exercise (i.e. 70% $VO_{2\ max}$) was not succesfull (Avery et al., 1997). Mottola et al. (1998b) investigated low-risk pregnant women and showed that mild exercise (30% HRR) on a stationary bike was better at promoting glucose tolerance in response to an oral glucose load after exercise than moderate intensity exercise (70% HRR) in late gestational women. Biopsies of the vastus lateralis muscle in these late pregnant women showed that total GLUT4 (glucose transporters sensitive to insulin) was elevated in the mild exercise–trained women (starting at 16–20 weeks gestation until delivery) compared with moderately trained women (Mottola et al., 1998a). Subsequently, when nutritional intake was controlled during pregnancy (to ~ 8350 kJ/day, with 200 g of carbohydrate/day), the combination of nutritional control and mild exercise (30% HRR on a stair climber) was better than mild exercise alone in controlling blood glucose concentrations and preventing excessive weight gain during pregnancy. This effect remained at 2 months postpartum (Mottola et al., 1999).

The above studies provided groundwork for development of a Nutrition and Exercise Lifestyle Intervention Program (NELIP), in which a mild walking program (30% HRR) was combined with nutritional control (8350 kJ/day; 200 g of carbohydrate/day) for women at risk for GDM (Sopper et al., 2004). Preliminary results are encouraging, in that women at risk for GDM did not develop this disease while on NELIP (N = 23), excessive weight gain was prevented, and normal glucose tolerance remained at 2 months postpartum (Batada et al., 2003). In addition, pregnant women at risk for GDM on NELIP maintained an insulin sensitivity index similar to those at low risk for GDM, and none developed GDM (Mottola et al., 2005b). It is suggested that overweight women at risk for GDM can be given a NELIP at 16 weeks of pregnancy to maintain insulin sensitivity and glucose excursion and to prevent excessive weight gain and GDM. Assessment of HbA 1c in these women also showed values well below the diabetic range (Mottola et al., 2005a). Studies conducted by our lab suggest that mild exercise, regardless of modality (bike, stair climber, or walking), may be a key factor—in combination with nutritional control—in helping women at risk for GDM and those women diagnosed with GDM, regulate blood glucose concentrations and prevent excessive weight gain during pregnancy.

4. Summary and recommendations

Obesity and type 2 diabetes are reaching epidemic proportions in society today and women of childbearing age are at risk for developing these diseases because of excessive weight gain during pregnancy and weight retention after birth. If modifiable risk factors for developing diabetes during pregnancy, such as preventing excessive weight gain and preserving glucose tolerance, can be reduced by incorporating physical activity, then exercise can be used as a powerful tool to reduce the diabetes and obesity epidemics in successive generations. Unfortuately, researchers have not be able to suggest an evidence-based program with guidelines for frequency, intensity, time and type of activity (FITT principal for exercise presciption) that would produce the best possible outcomes for women with GDM. Although preliminary results are encouraging, exercise is still considered an adjunctive therapy, and the true effectiveness of a specific exercise program in controlling glucose excursion and reducing the incidence of insulin therapy remains untapped.

Based on the literature reviewed, it is suggested that in using the FITT principal of exercise prescription, women who are at risk for or who have been diagnosed with GDM, should engage in activity at a frequency of 3-4 times per week, for at least 25 minutes each session, at a mild intensity (walking pace), building to 40 minutes, would be sufficient to provide health benefits. In addition, it is suggested that if pedometers are available, 10,000 steps per day may also regulate glucose metabolism. If women with GDM are overweight or obese, a target heart rate of 102-124 beats per minute (20 to 29 years of age) and 101 to 120 beats per minute (30 to 39 years of age) may also be used to monitor intensity. Continuing research is necessary in this important field especially if new stringent cut-offs for diagnoses of GDM are adopted as guidelines, as they will cause a higher prevalance of GDM, increasing the cost of medical care. Prevention of GDM by adoption of a healthy lifestyle and active living may be key.

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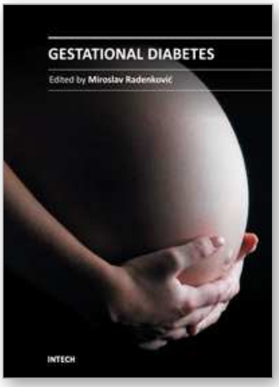

Gestational Diabetes

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Gestational diabetes mellitus is defined as hyperglycemia with onset or first recognition during pregnancy. The incidence of gestational diabetes is still increasing and this pathological condition has strong association with adverse pregnancy outcomes. Since gestational diabetes can have long-term pathological consequences for both mother and the child, it is important that it is promptly recognized and adequately managed. Treatment of gestational diabetes is aimed to maintain euglycemia and it should involve regular glucose monitoring, dietary modifications, life style changes, appropriate physical activity, and when necessary, pharmacotherapy. Adequate glycemic control throughout the pregnancy can notably reduce the occurrence of specific adverse perinatal and maternal outcomes. In a long-term prospect, in order to prevent development of diabetes later in life, as well to avoid associated complications, an adequate education on lifestyle modifications should start in pregnancy and continue postpartum.

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