Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Amy Memmer Date

Lifestyle interventions for the prevention and management of gestational diabetes mellitus among Latinas

By

Amy Memmer
Master of Public Health

Hubert Department of Global Health

_____

Mohammed K. Ali, MBChB, MSc, MBA
Committee Chair

Lifestyle interventions for the prevention and management of gestational diabetes mellitus among Latinas

By

Amy Memmer

B.S., University of California Santa Barbara, 2010

Thesis Committee Chair: Mohammed K. Ali, MBChB, MSc, MBA

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Hubert Department of Global Health
2015

Abstract

Lifestyle interventions for the prevention and management of gestational diabetes mellitus among Latinas
By Amy Memmer

OBJECTIVE: Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy and it is more common among minority groups (e.g., Latina women) compared to non-Hispanic white women. GDM increases the risk of multiple fetal and maternal perinatal outcomes, and increases a woman's subsequent risk of type 2 diabetes by over seven-fold. Studies of lifestyle interventions to prevent GDM and its related perinatal outcomes have conflicting results, and few studies have included Latinas. This review and meta-analysis aimed to identify what is currently known about the effectiveness of lifestyle interventions and exposures for prevention and management of GDM among Latinas.

METHODS: A systematic review of the literature was performed by searching PubMed, CINAHL, Web of Science, EMBASE, CENTRAL, and ClinicalTrials.gov databases for studies published in English or Spanish using key words relating to three elements: 1) GDM, 2) lifestyle exposures/interventions (primarily diet and exercise), and 3) the population of Latinas living in the Americas. Observational and experimental studies that addressed all three elements and provided data on the outcomes of interest were considered eligible for inclusion. Meta-analysis was carried out using a fixed effects model to provide summary odds ratios and the I^2 assessment of heterogeneity.

RESULTS: The search returned 1647 relevant articles, from which 6 original studies were included in this review. There were no statistically significant relationships between Latinas' reported levels of physical activity in pre-, early, or mid-pregnancy and the risk of developing GDM. Due to heterogeneity of study designs and outcomes, meta-analysis was only performed for the relationship between physical activity levels and the risk of GDM.

CONCLUSIONS: This systematic literature review identified a dearth of studies of lifestyle interventions for prevention and management of GDM that include Latina populations. Although this meta-analysis found no significant association between reported levels of physical activity and risk of GDM, it was limited to two observational studies of physical activity amongst pregnant Latinas, and more research is needed on this topic.

Lifestyle interventions for the prevention and management of gestational diabetes mellitus among Latinas

By

Amy Memmer

B.S., University of California Santa Barbara, 2010

Thesis Committee Chair: Mohammed Ali, MBChB, MSc, MBA

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Hubert Department of Global Health
2015

Acknowledgements

I would like to thank my thesis advisor, Dr. Mohammed Ali for his enthusiasm, support, and mentoring throughout this long process. I was fortunate to find an advisor who was willing to work with me via phone calls and emails while I was completing my thesis and medical degree on the other side of the country. I would also like to thank Dr. Felipe Lobelo for his support in the brainstorming process and for helping me to identify such an interesting area of diabetes prevention research. My time at Rollins School of Public Health was transformational in my understanding of health, and I am grateful for all of the support and mentoring I received during that time. A special thank you to Angela Rozo for her help and support.

Table of Contents

Chapter 1: Introduction

1.1 Background of the Problem

Type 2 diabetes mellitus. A long-standing problem in the United States, type 2 diabetes mellitus is now an increasingly common problem of low- and middle-income countries as well (Holub 2013). Type 2 diabetes mellitus causes multiple health complications including vascular disease and immune system dysfunction, which contribute to significant morbidity and mortality (ADA 2014a; Vincent 2014; CDC 2011). Type 2 diabetes mellitus is a widespread chronic disease that increases health care spending in many countries (Cosgrove 2002). In the United States, diabetes and its related health complications cost around $245 billion per year (CDC 2014). The global annual cost of preventing or treating diabetes mellitus is estimated at 418 billion U.S. dollars (Wendland 2011) and will increase as the number of people with diabetes mellitus grows (WHO 2015). Compared to those without diabetes mellitus, people with the disease spend about four times as much on healthcare (Cosgrove 2002). The economic problem of diabetes mellitus is compounded by the fact that diabetes and its complications are more common amongst racial/ethnic minorities, the elderly, and people with lower incomes (Ruggiero 2011).

Gestational diabetes mellitus. Gestational diabetes mellitus (GDM) is a separate problem of diabetes occurring only during pregnancy, however, it is well known to significantly increase a woman's risk of type 2 diabetes mellitus in the years following pregnancy (Coustan 2014; Kjos 1995). GDM is one of the most common complications of pregnancy (Chasan-Taber 2014a) and it has both short- and long-term implications for the health of mother and child (Coustan 2010). It is estimated that GDM increased national medical costs in the United States by $636 million in 2007, which is over $3,000 more per GDM-affected pregnancy compared to non-GDM affected pregnancy. This estimate does not include the costs associated with the increased prevalence of type 2 diabetes that is attributable to GDM (Chen 2009).

Global health implications of GDM prevention and management. When the epidemiology, morbidity, and economic and social impacts are considered together, it becomes clear that GDM prevention is a relevant issue for public health. Pregnancy is identified as an opportune time for disease

prevention because of the unique situation it presents (Wendland 2011). It is a time in most women's lives when they seek regular medical care, undergo screening for multiple conditions, and are typically willing to take better care of their health (Artal 2014). Prevention or better management of GDM may be a means of primary prevention of type 2 diabetes in women and their children who would be at high risk for type 2 diabetes after a pregnancy complicated by GDM (Chasan-Taber 2014a). This could significantly reduce global mortality, since diabetes is one of the top four leading causes of death by non-communicable diseases worldwide (WHO 2015b). By lowering perinatal mortality, prevention of GDM and its associated perinatal complications could also improve child health indicators such as those used in the Millenium Development Goals (Benhalima 2014; Wagner 2004; United Nations 2008).

GDM prevention and management. Experts believe that prevention of GDM could prevent or delay the onset of one in every six new cases of type 2 diabetes mellitus (Chasan-Taber 2014a). The pathophysiology of GDM is similar to type 2 diabetes mellitus and it has been hypothesized that type 2 diabetes prevention methods may also prove effective in preventing GDM (Oostdam 2011). Diet and exercise are recognized methods for preventing the onset of type 2 diabetes (Knowler 2002), but there is less conclusive research about diet and exercise for the prevention of GDM (Oostdam 2011; Hawkins 2014; Ruchat and Motolla 2013). This is of concern because diet and exercise are the only means of controlling gestational diabetes to date other than insulin treatment, and oral hypoglycemic medications are not approved by the FDA for treatment of GDM in the U.S. (Artal 2014; Jovanovic 2004; Coustan 2015).

The evidence for health benefits from detection and management of GDM is so strong that the U.S. Preventive Services Task Force recommends screening all asymptomatic pregnant women after 24 weeks of gestation for GDM (Moyer 2014). Although there is good evidence to support screening and treatment for GDM, less research has focused on prevention of GDM and its associated perinatal complications (Han 2012; Han 2013). The literature is even scarcer on this topic in regards to minority racial/ethnic groups such as Latinas, who have an elevated risk of diabetes and GDM compared to non-Hispanic white women (Fujimoto 2013). Latinas are part of the largest racial/ethnic minority group in the

United States and have one of the highest fertility rates (CDC 2015; McDonald 2008). They also tend to have higher body mass indices (BMI) upon starting pregnancy and lower levels of physical activity during pregnancy compared to non-Hispanic white women (Chasan-Taber 2014a; Chu 2009; Petersen 2005).

GDM in the Latino population. Knowledge of the effectiveness of lifestyle interventions among Latinas is important because GDM prevention may be more effective if targeted towards high-risk subgroups of the population. Latino and Hispanic are terms that are externally-applied to diverse populations of people deriving from Latin America and Spanish-speaking countries, respectively (Calderon 1992; Passel and Taylor 2009). The term Latino is used in this review, as the populations of interest to this study are those living within the Americas. The people grouped into these broad categories are very different, and even when living in the U.S., their families originate from many different countries (Passel and Taylor 2009). Subgroups of this population may have significant differences in health outcomes and GDM research shows variations in the incidence of GDM among subgroups of the Hispanic/Latino population in the U.S. (Fujimoto 2013). Research on GDM prevention among Hispanic/Latina women is in the early stages and future research should determine the best approach to preventing GDM in high-risk groups within the broader umbrella of "Latino."

1.2 Statement of the Problem

The findings of research on lifestyle interventions for prevention and management of GDM are conflicting, and few studies have included Latinas (Fujimoto 2013). The consequence of this knowledge gap is that healthcare providers and their pregnant patients do not have evidence-based information about what lifestyle interventions are effective in preventing GDM and its related perinatal complications. Knowledge about what lifestyle changes are effective could help prevent many cases of GDM, its associated health complications, and subsequent cases of type 2 diabetes mellitus.

1.3 Statement of Purpose

The purpose of this systematic literature review is to:

- Summarize the current evidence regarding associations between lifestyle exposures and the risk of GDM and its perinatal complications among Latinas
- Determine the incidence of GDM occurring in Latinas
- Evaluate the quality of evidence on these topics
- Identify specific needs for future research on this topic

1.4 Research Questions

This systematic literature review seeks to answer the following questions:

1. Are lifestyle exposures associated with the risk of developing GDM and its related perinatal complications among Latinas?
2. Is *physical activity* associated with reduced risk of GDM or its perinatal complications? If so, what type of exercise, what duration, and what frequency of exercise is effective in reducing the risk of GDM/GDM-related perinatal complications?
3. Is a healthier *diet* associated with reduced risks of GDM or its perinatal complications? If so, what type and amount of diet is effective in reducing the risk of GDM/GDM-related perinatal complications?
4. Is there another lifestyle behavior or combination of factors that is/are associated with reduced risks of GDM or its perinatal complications?
5. Is there a specific time period before or during pregnancy in which lifestyle interventions are effective at lowering the risk of GDM/GDM-related perinatal complications?

Based on preliminary review of the literature, our hypothesis was that higher levels of physical activity and intake of lower glycemic-index (GI) foods during the first half of pregnancy would be associated with lower risk of GDM in Latinas as compared to lower physical activity levels and intake of higher glycemic-index foods.

1.5 Statement of the Significance

Medical professional groups like the American College of Obstetricians and Gynecologists endorse general diet, exercise, and weight gain recommendations during pregnancy but there is a lack evidence to provide specific recommendations for prevention of GDM (Han 2012; Jovanovic 2004; Artal 2003). Previous systematic reviews included studies of largely non-Hispanic white, European, or Australian women that lack generalizability to minority racial/ethnic populations (Han 2012; Han 2013; Tieu 2011; Oostdam 2011; Tobias 2011). A systematic review on this topic as it pertains to the Latino population is important because of the issue of generalizability. Latinas are a particularly vulnerable population for GDM and type 2 diabetes mellitus (Fujimoto 2013). Research that has been done and summarized on the topic of gestational diabetes prevention is not clearly generalizable to this important segment of the population. Future research, policies, and health interventions may be more effective when informed by research that targets higher risk groups, particularly because those groups may have specific cultural and socioeconomic needs.

This systematic literature review aims to identify what is currently known about the effectiveness of lifestyle interventions for prevention and management of GDM among Latinas, and where there are still gaps in our knowledge. The meta-analysis combines data from relevant studies to statistically analyze the relationship between lifestyle exposures and the risk of GDM or related perinatal outcomes. Where there is insufficient evidence on this topic, this review will highlight specific needs for future research. Addressing this knowledge gap is important because prevention of GDM in the Latino population could prevent the associated short- and long-term complications of GDM in a population with an elevated risk of diabetes. The downstream effects could be a decrease in healthcare spending, the risk of perinatal mortality, macrosomia, preeclampsia, cesarean deliveries, and the prevalence of type 2 diabetes mellitus in the U.S. and Latin America (Chasan-Taber 2014a; Coustan 2010; Chu 2009; Benhalima 2014; Ostlund 2004).

1.6 Definition of Terms

- Gestational Diabetes Mellitus: Glucose intolerance with onset during pregnancy (Benhalima 2014).
- Type 2 Diabetes Mellitus: a metabolic disorder characterized by elevated blood glucose levels that arises due to insulin resistance usually accompanied by relative insulin deficiency (ADA 2014a).
- Abnormal Glucose Tolerance: An abnormal response to glucose, in which a woman's blood glucose level is greater than 135 mg/dL 1 hour after a 50 gram oral glucose challenge. This means the woman screened positive on the first part of a two-step GDM screen (Chasan-Taber 2014b).
- Latina: Female who traces her origin to a country in Latin America and the Caribbean, including Mexico, Central America, and South America (Calderon 1992; Passel and Taylor 2009; World Bank 2015).
- Lifestyle intervention: May consist of changes in diet or physical activity, as opposed to a primarily medical intervention such as medication or surgery.
- Macrosomia: Fetal growth beyond 4,000 or 4,500 grams, regardless of gestational age (Chatfield 2001).
- Large for Gestational Age (LGA): describes an infant with a birth weight greater than the 90th percentile for that gestational age (Mandy 2014).

Chapter 2: Comprehensive Review of the Literature

2.1 Introduction

In order to demonstrate the importance of research on GDM prevention and management in Latinas, this literature review highlights the problems posed by GDM and their particular relevance to Latinas. This literature review includes a summary of the major findings from systematic literature reviews on the prevention and management of GDM, which were identified from searching the Cochrane Library and PubMed database. It also highlights the major knowledge gaps identified by these systematic reviews. One important gap is the lack of inclusion of Latinas in the research on GDM prevention and management. One of the most prolific groups working on GDM research in Latinas is led by epidemiologist Dr. Lisa Chasan-Taber at the University of Massachusetts, Amherst. Baystate Health in Western Massachusetts has recruited several cohorts of predominantly Puerto Rican pregnant Latinas, from which Chasan-Taber et al. have collected their data (Chasan-Taber 2008; Chasan-Taber 2014b). These studies, as well as the others identified from the systematic search of the literature are described in more detail in Chapter 3.

2.2 Prevalence of GDM

One study of a multi-ethnic patient group in the U.S. found that the prevalence of GDM doubled from 2.1% to 4.1% between the years 1994 and 2002 (Dabelea 2005). Although the prevalence of GDM has been cited at 2 to 5% (Chasan-Taber 2008), it is predicted that 18% of pregnancies will be affected by GDM based on new international consensus guidelines for GDM diagnosis (Chasan-Taber 2014a). The risk of GDM is greatest for minority ethnic/racial groups such as Latinas. Within the Latina population, the prevalence of GDM is higher in women of Mexican and Puerto Rican heritage (6.0% and 5.3%, respectively) than women of Central American, South American, or Cuban heritage (4.6, 4.4, and 4.0%, respectively) (Fujimoto 2013). The higher risk of GDM seen in Mexican Americans is paralleled by a higher GDM prevalence of 8-12% among pregnant women in Mexico (Perichart-Perera 2012).

2.3 Risk factors for GDM

GDM usually occurs after 20 weeks gestation, when the placenta releases hormones that alter the mother's metabolic state to increase glucose delivery to the fetus. Women whose bodies are less able to handle the resultant increased hyperglycemia may develop glucose intolerance. Known risk factors for GDM are higher BMI, older maternal age, prior history of GDM, family history of type 2 diabetes mellitus in a first-degree relative, and metabolic syndrome (AHRQ 2012).

2.4 Health Outcomes of GDM

GDM has important consequences for the health of mother and child (Metzger 2007). Poorly controlled GDM is associated with a four-fold higher risk of infant mortality (Fujimoto 2013). A large, international multi-center study called HAPO (Hyperglycemia and Adverse Pregnancy Outcome Study) found that there was a continuous association between maternal glucose levels and fetal growth-related outcomes, even at glucose levels deemed "normal." This finding highlights the importance of improving glycemic control during pregnancy to promote a healthy intrauterine environment, as this will affect fetal body composition, fetal insulin levels (Coustan 2010), and perhaps the child's lifelong risk of diabetes (Boney 2005; Crume 2011). It also highlights the need to evaluate biological differences in the degree of the maternal glucose-fetal growth relationship among different population groups, since some ethnicities/races seem more predisposed to glucose intolerance (Fujimoto 2013). The HAPO study confirmed the finding identified in many other studies, that GDM increases the risk of several outcomes affecting the health of mother and fetus (Coustan 2010).

Macrosomia and large-for-gestational-age. Low birth weight is used as an indicator of maternal and child health, however, high birth weight also poses health problems for mother and neonate (Kieffer 2006). Macrosomia is a term meant to indicate that an infant's birth weight is excessive. Some define macrosomia as a birth weight greater than the 90th percentile for gestational age (Coustan 2010), however, this definition is used interchangeably for infants deemed large-for-gestational age (LGA). Other definitions of macrosomia include birth weight cutoffs of greater than 4,000 or 4,500 grams (Chatfield 2001). Regardless of the definition used, macrosomia and LGA are both more common in

neonates of women with GDM compared to those born to women without GDM (Wendland 2011; Jovanovic 2004; Bowers 2013). The relationships between GDM, LGA, and poor birth outcomes were found to be independent of pre-pregnancy obesity and pregnancy weight gain. The combination of pre-pregnancy obesity, excessive pregnancy weight gain, and maternal GDM more than doubled the risk of infants born LGA to Latinas (Bowers 2013). Macrosomia and LGA of the neonate increase the risk of injury to the mother and infant during delivery (Jovanovic 2004). LGA increases the risk of shoulder dystocia (fetus' shoulder stuck in the birth canal making delivery difficult) and cesarean deliveries (Benhalima 2014; Baxley and Gobbo 2004). It also increases the risk of neonatal hypoglycemia and mortality (Siega Riz 2009).

Cesarean delivery. The higher incidence of macrosomia and LGA in fetuses of GDM pregnancies helps explain why the risk of cesarean deliveries (c-sections) is also higher in women with GDM (Wendland 2011). However, the diagnosis of GDM itself may lead to more planned cesarean deliveries. One study found that even when GDM was treated and the fetus was not macrosomic, the rate of cesarean deliveries remained higher among women with GDM than women with normoglycemic pregnancies (Naylor 1996). The relationship of GDM and cesarean deliveries is important because cesarean deliveries, even when planned, impart a higher risk of the neonate requiring intensive care and having early pulmonary problems compared to vaginal deliveries (Kolas 2006). Planned cesarean deliveries also increase a woman's risk of requiring re-hospitalization within 30 days of delivery and increase healthcare costs compared to planned vaginal deliveries (Declercq 2007).

Preeclampsia. Like GDM, hypertensive disorders of pregnancy are a group of disorders that occur only during pregnancy. Several studies show an association between GDM and the risk of hypertensive disorders of pregnancy (Coustan 2010; Ostlund 2004; Bryson 2003). Preeclampsia is one of the most common hypertensive disorders in pregnancy, and is defined as the onset of high blood pressure and protein in the urine after 20 weeks gestation. Preeclampsia can cause organ damage in the mother, premature delivery, and growth restriction and death in the fetus (Bryson 2003). There is no effective prevention method for preeclampsia and once it develops, the only definitive treatment is delivery of the

fetus (Wagner 2004). GDM may increase the risk of preeclampsia up to three-fold compared to women without GDM (Ros 1998). More severe GDM is associated with an increased rate of preeclampsia and the effect is independent of BMI (Yogev 2004; Ostlund 2004).

Obesity and diabetes in offspring. Children of pregnancies affected by GDM seem to be at higher risk of developing obesity and glucose intolerance later in life compared to children of pregnancies not affected by GDM (Crume 2011; Davis 2013). One study followed a cohort of children from GDM and non-GDM pregnancies until age 11 and found that children who were born LGA to mothers with GDM were more likely to develop metabolic syndrome during childhood compared to appropriate size-for-gestational age infants not from pregnancies with GDM. However, this study did not find that GDM independently increased the risk of metabolic syndrome among the children (Boney 2005) and other studies on this topic have likewise found conflicting results (Crume 2011). One cohort study did find a positive association between GDM exposure in utero and adiposity changes in Latinos during puberty. Davis et al. looked at this effect in Latino children and found that GDM-exposed children had greater increases in total body fat and greater decreases in insulin response during puberty compared to non-GDM children (Davis 2013). However, their analysis did not adjust for maternal pre-pregnancy BMI, which has been found to attenuate the relationship between GDM and childhood obesity (Crume 2011). Investigation of the relationship between maternal diabetes/GDM and childhood obesity is important, because a similar trans-generational phenomenon independent of maternal obesity has been observed to contribute to the high risk of diabetes in Pima Indians (Pettitt 1983). If this is found to be the case for Latinos, it will give even greater importance to the prevention of GDM among Latinos.

Diabetes after pregnancy. One of the most well-known impacts of GDM is an increase in risk of type 2 diabetes for women after a diagnosis of GDM. Studies suggest that GDM increases a woman's risk of developing type 2 diabetes by as much as seven-fold and that 50% of women will develop type 2 diabetes within 5 years of having GDM (Kjos 1995). This strong relationship demonstrates the importance of preventing GDM, because it may prevent or delay onset of type 2 diabetes. Better glucose control in GDM may also reduce the incidence of type 2 diabetes among women, as it has been observed

that an elevated fasting blood glucose level during a GDM-affected pregnancy is associated with subsequent risk of type 2 diabetes (Kim 2002). Such evidence has led the American Diabetes Association to recommend lifelong screening for diabetes for women with prior GDM at least every three years (ADA 2014b). Compared to non-Hispanic white women with GDM, Latinas with GDM have an increased risk of developing type 2 diabetes, even after controlling for pre-pregnancy BMI and other confounders (Fujimoto 2013). This heightened predisposition towards type 2 diabetes after GDM highlights the importance of preventing GDM in Latinas.

2.5 Prevention & Management of GDM

Several systematic reviews and meta-analyses over the past ten years have looked at various lifestyle interventions for prevention or management of GDM. The majority of these reviews were performed by a group of researchers in the Australian Research Centre for Health of Women and Babies (Han 2012; Han 2013; Tieu 2011). Most of the studies included in these and other systematic literature reviews of GDM prevention include primarily non-Hispanic white women. The reviews mainly differ in the interventions and outcomes they include, however, a common conclusion is that the methodological quality of studies is generally low and sample sizes of studies are often small. The reviews, the interventions they evaluated, and their findings are summarized here.

Dietary Interventions. Diet is one of the mainstays of GDM management (Jovanovic 2004) and is also thought to be a means of preventing GDM and its related outcomes (Tieu 2011). The plausibility of this hypothesis is supported by the evidence that diabetic fetopathy (hyperglycemia, hyperinsulinemia, and macrosomia) can be reduced by blunting the mother's peak blood glucose levels after meals. However, there are insufficient randomized controlled trials supporting specific dietary recommendations for prevention or management of GDM (Han 2013; Tieu 2011). The following reviews and meta-analyses looked at specific dietary interventions and their effectiveness in preventing GDM or related adverse perinatal outcomes.

Tieu et al. looked at trials of dietary interventions for the prevention of GDM. They found that women on a low glycemic index (GI) diet had lower fasting blood glucose levels and lower risk of having

large-for-gestational-age infants, however, their review included only three trials with a total of 107 women. Low GI diet was only compared to high GI diet in the included trials (Tieu 2011). A more recent systematic review of nine trials with 884 women by Vercoza Viana et al. also found that low GI diets reduced the use of insulin in women with GDM and reduced newborn birth weight. The authors estimated that 13 out of 100 women with GDM would not need to use insulin if they followed a low GI diet. The review found that low carbohydrate diets did not seem to reduce insulin use, cesarean deliveries, or newborn size. Likewise, total energy restriction diets did not affect rates of macrosomia or neonatal hyperglycemia, but evidence was lacking for other outcomes such as insulin use (Vercoza Viana 2014).

Han et al. of the Australian research group performed a systematic review of the effect of dietary advice for women with GDM on the risk of various pregnancy outcomes. They included nine trials with 429 women and analyzed pairwise comparisons between different types of diets. None of the comparisons showed a significant difference in the risk for the perinatal outcomes of interest, such as c-sections or macrosomia, and the studies had small sample sizes. Like Tieu et al., the authors of this review conclude that more studies are needed in order to make a recommendation for dietary interventions (Han 2013).

The current evidence suggests that low GI diets may be more effective than other diets at improving maternal glucose control and preventing LGA (Tieu 2011; Vercoa Viana 2014). Limitations of the research on this topic include few randomized controlled trials, small sample sizes, limited reporting of data on relevant clinical outcomes, and difficulty of measuring adherence to diet. Among the three reviews discussed, only one review included a study with a Latina population (Vercoza Viana 2014).

Physical activity interventions. The Diabetes Prevention Program study and its subsequent community applications show the importance of both diet and exercise in the prevention of type 2 diabetes among high-risk populations (Knowler 2002; Ockene 2012). As with prevention of type 2 diabetes, exercise in pregnancy may reduce the risk of gestational diabetes by increasing the sensitivity of skeletal muscle to insulin, decreasing oxidative stress, increasing beta-cell function, and by changing body composition (Han 2012; Hawkins 2014). Regular physical activity is now a routine recommendation

for pregnant women (Artal 2003), but the timing, intensity, and type of activity that is most effective for prevention of GDM and its related outcomes has yet to be determined.

Tobias et al. reviewed the literature on physical activity before and during pregnancy for the prevention of GDM. They included eight studies with over 34,000 women and found that higher levels of total physical activity in pre-pregnancy and early pregnancy reduced the odds of developing GDM compared to lower levels of physical activity (pooled OR=0.45, 95% CI 0.28-0.75). For the total physical activity variable, no information on the specific activity or its frequency, duration, or intensity was reported. The authors found similar statistically significant reductions in GDM risk for the highest levels of activity in brisk walking, stair climbing, and vigorous activity in pre-pregnancy. The pre-pregnancy time period of the studies ranged from several years to three months prior to the index pregnancy, so it needs to be elucidated how much physical activity prior to pregnancy effectively reduces the risk of GDM. Tobias et al. point out that it remains unknown whether pre-pregnancy, early pregnancy, or both are the critical times for physical activity, since pre-pregnancy physical activity predicts a woman's physical activity in early pregnancy. The authors found no randomized controlled trials meeting inclusion criteria, demonstrating that research on the topic is relatively sparse (Tobias 2011).

Another systematic review of exercise and risk of GDM by Han et al. included five studies (1,115 women) that were identified in clinical trial registries. The authors found no significant difference in the incidence of GDM or insulin sensitivity for women receiving exercise interventions compared to those receiving routine prenatal care. However, the majority of the studies had small sample sizes. Like Tobias et al., Han et al. conclude that there is insufficient evidence to guide the use of exercise for preventing gestational diabetes, and that there is a need for more rigorous studies on the topic (Han 2012).

A more limited review of physical activity interventions and the risk of gestational diabetes found three studies that showed improvement of glucose tolerance and insulin sensitivity. Despite significant improvement in glucose tolerance, none of these studies observed a difference in the risk of GDM between groups. As with many small studies of GDM, the incidence of GDM was small and these studies were not powered to analyze the risk of GDM. The interventions that seemed to improve glucose

tolerance ranged from total energy expenditure goals to biweekly aerobic and weekly aquatic exercise sessions. All three studies achieved good compliance with the intervention, which may account for their success. Compliance was an issue in most of the studies that did not observe significant differences in glucose tolerance and insulin sensitivity. The review also looked at management of GDM and found that the majority of studies observed improvement of glycemic control or reduction in insulin use with the exercise intervention. Some of these studies included nutrition as a co-intervention with exercise, so the effectiveness of exercise alone on GDM management is less clear (Ruchat and Mottola 2013).

Combined & miscellaneous interventions. Many studies investigate combinations of diet and exercise, which make it more difficult to pinpoint which intervention was effective. Oostdam et al. observed this in their systematic literature review and meta-analysis of controlled trials for the prevention of GDM. They included a more diverse range of interventions compared to other reviews and identified 19 studies meeting inclusion criteria. They found that only dietary counseling significantly reduced the incidence of GDM in the intervention groups compared to the control groups. The dietary counseling in the studies included advice on lowering energy intake or reducing weight gain, but it varied in other aspects. The review also found that women who were advised on a low GI diet had a lower risk of having an LGA newborn compared to women with high GI diets. Conclusions on these findings are somewhat limited because the nine studies that looked at dietary counseling had heterogeneous co-interventions that may have modified the effect. This review found no trials that compared a LGI diet to usual care, so the authors could draw no conclusions about the effectiveness of a LGI diet on reducing the incidence of GDM. The authors conclude that the quality of evidence for the included studies is low and that there is no clear best intervention for the prevention of GDM (Oostdam 2011). Despite the broad inclusion criteria for this review, it included no studies with predominantly Latina women.

Hawkins et al. recently published a randomized controlled pilot study (N=68) of a lifestyle intervention for prevention of GDM risk factors in overweight and obese pregnant Latinas. The intervention consisted of six, monthly in-person and five phone counseling sessions during pregnancy. Women were advised to exercise at least 30 minutes every day for most days of the week, according to

American College of Obstetricians and Gynecologists guidelines. For diet, they were advised to follow American Dietetic Association recommendations of less high saturated fat and more fiber. Both the primary outcomes, diet and exercise, were self-reported. The study found that women in the intervention group increased vigorous-intensity physical activity while women in the standard care group decreased vigorous-intensity activity during pregnancy (mean difference=2.3 MET-hours/week, p=0.04). Despite this finding, there were no statistically significant differences between groups in the average amount of gestational weight gain, infant birth weight, or markers of insulin resistance. Given that physical activity tends to decline during pregnancy, the fact that women in the intervention group slightly increased vigorous-intensity activity suggests promise for such an intervention during pregnancy. This study may also prove a good model for future interventions with Latinas, as it saw good retention and follow-up for participants (Hawkins 2014).

2.6 Qualitative Research

Research on the risk and prevention of GDM among Latinas is limited. The biological mechanism of diet and exercise in the prevention of GDM should not differ between different races or ethnicities, however, the feasibility and adaptation of such interventions may be affected by socio-cultural nuances. Cultural nuances, whether or not they affect uptake of GDM prevention interventions, limit the ability to generalize findings from research in non-Latino populations. Additionally, diet or exercise levels may need to be adjusted for groups that are more physiologically prone to glucose intolerance at baseline. Understanding the breakdown in risk for GDM and the effectiveness of prevention interventions among different Latino subgroups is important for targeting prevention efforts for groups of the population that are most at risk. The remainder of this chapter will summarize qualitative studies of lifestyle interventions and knowledge, attitudes, beliefs, and practices of pregnant Latinas in order to provide some background on the cultural aspect of the topic.

Several qualitative studies have investigated the facilitators and barriers that women face when becoming healthier during pregnancy. Access to advice from medical experts may be one of these barriers. Several studies suggest that in order to ensure the health of their babies, Latinas are willing to

follow the advice of medical experts regarding diet and exercise (Ferrari 2013; Rhoads-Baeza and Reis 2010). One qualitative study of a diverse sample of pregnant women and their attitudes towards lifestyle advice from healthcare providers found that Hispanic women seemed the most receptive to dietary advice from healthcare providers. In regards to advice on physical activity during pregnancy, the study found that most women, Latinas included, were dissatisfied and felt that they were not receiving enough information from healthcare providers (Ferrari 2013).

Other sources of information and cultural influence may both facilitate and prevent healthy behaviors during pregnancy. Thornton et al. interviewed pregnant and postpartum Latinas in Detroit. In this population they found that women relied heavily on their husbands for information and emotional support for diet and exercise during pregnancy. The interviews revealed women's motivation for maintaining a healthy weight during pregnancy, which included their husbands' advice and opinions of them, and a desire to have a healthy or "big" baby. The study also found that cultural beliefs and family rituals shaped diet and exercise behaviors. For example, women indicated that they felt obliged to eat less healthy diets when the family wanted to eat out or when at a social gathering (Thornton 2006). Based on these findings, it may be beneficial to involve women's social support networks in the design of lifestyle interventions.

Certain barriers and facilitators of healthy lifestyles during pregnancy may be more important for Latinas compared to other population groups. Marquez et al. found that the barriers and facilitators to exercise during pregnancy differed in some respects for Latinas and non-Hispanic white women. For example, Latinas highly valued information and proper diet as facilitators for them to exercise. On the other hand, both groups identified common barriers to exercise, such as physical limitations and lack of energy. The authors aptly point out that their findings cannot and should not be attributed to ethnicity, but the findings may be useful in informing the design and implementation of tailored exercise interventions (Marquez 2009).

Rhoads-Baeza and Reis performed a mixed methods investigation of pregnant women's understanding of GDM and diet change. It was a study of predominantly low-income, Mexican American

women in Illinois. The quantitative portion of the study consisted of a survey to assess women's level of knowledge and opinions on GDM and prenatal health. Regarding diet, most women (85%) correctly answered questions about eating fruits and vegetables, whereas only 51% correctly answered that controlling carbohydrate intake could improve pregnancy outcomes. The majority of women did not seem to understand the relationship between sugar and GDM, or obesity and GDM. Consistent with other studies, they found that the women were overwhelmingly willing to make efforts to ensure the health of their babies, and that women followed recommendations of their physicians and wanted more information about how to be healthy. However, most women felt that diet change was difficult and also agreed with the statement that fate plays a role in determining who gets diabetes, regardless of their lifestyle changes. This idea of destiny also came up as a key theme in the interview portion of the study. The interview revealed eight key themes about challenges and facilitators to having a healthy pregnancy. Of note, all 48 women interviewed expressed pregnancy as a motivator for them to become healthier. Family, routine, and cost of food were identified as important factors that affect diet. A majority of the women expressed fear about diabetes and how eating sugar could cause diabetes. The interviews also revealed interesting opinions on how to improve women's diets. For example, women wanted to involve the whole family in the changes, thought that eating less tortillas would not be feasible, and expressed interest in a cooking class (Rhoads-Baeza and Reis 2010).

2.7 Summary

In summary, GDM is a problem of increasing prevalence with many short- and long-term health complications for mother and child. Prevention and improved management of GDM is important to prevent these complications. GDM imparts a significantly higher risk of type 2 diabetes for women after pregnancy, so prevention of GDM may prevent or delay the onset of type 2 diabetes as well. This relationship is particularly important among Latinas, who have an increased risk of GDM compared to non-Hispanic white women. Healthy diet and exercise are recommended for women during pregnancy, however, there is not enough evidence to recommend a particular diet or exercise regimen for the prevention of GDM. This knowledge gap is even greater for the Latino population, because few studies

on this topic have included Latinas. Qualitative research suggests that Latinas are eager to be healthy during pregnancy for the sake of their babies and they desire more information about proper diet and exercise. There is a need to identify, summarize, and evaluate all research on the prevention and management of GDM in Latinas, to determine if there is evidence for effective dietary or physical activity advice in this population. The status of research on this topic is best assessed by a systematic review of the literature, which will identify what knowledge gaps still exist.

Chapter 3: Methods & Results

3.1 Methods

Introduction. A systematic review of the literature was performed to help answer and better define the knowledge gap regarding prevention and management of GDM among Latinas. A brief review of the literature on this topic (see Chapter 2) returned several systematic reviews, with some evidence for the effectiveness of certain dietary and physical activity interventions, yet very few studies from these reviews included Latinas. A systematic literature review was chosen to address this knowledge gap in order to identify literature specific to the population, interventions, and outcomes of interest, as well as to summarize findings of the current literature on this topic as it pertains to Latinas. A meta-analysis was performed to increase the precision and power to detect a significant relationship between variables of interest.

Population. The population chosen for this review consists of Lat**i**nas in the Americas, including the United States, Mexico, Central and South America, and the Caribbean Islands. Latina women were the focus of this review because they are at higher risk for gestational diabetes compared to non-Hispanic white women. They are also the largest minority group in the U.S., the fastest growing population group, and have one of the highest birth rates (CDC 2015; Chasan-Taber 2014b). Studies from all American countries were included because these countries have significant Latino populations and their inclusion increases the sensitivity of the review to detect studies with relevant findings.

Study selection. Database searches were carried out in PubMed, CINAHL, Web of Science, EMBASE, CENTRAL, and ClinicalTrials.gov from database inception until June 30, 2014. Only studies in English and Spanish language were eligible for inclusion. The search strategy was based on major themes and keywords related to: 1) gestational diabetes mellitus or abnormal glucose tolerance, 2) lifestyle interventions (such as diet and exercise), and 3) the population of Latinas in the Americas. Studies considered for inclusion had to contain these three elements and either be comprised of at least 50% Latinos or stratify results for race/ethnicity. Study designs considered for inclusion were randomized

controlled trials, quasi-experimental studies, pre-post studies, prospective cohorts, and retrospective cohorts.

The databases were searched for primary investigations using the following search terms as free text and medical subject heading (MESH) terms for the outcomes, interventions, and population of interest:

> (gestational diabetes OR prediabetes OR hemoglobin a1c OR impaired glucose tolerance OR abnormal glucose tolerance OR oral glucose tolerance test OR fasting blood glucose OR fasting blood sugar OR impaired fasting blood glucose OR oral glucose challenge test OR random blood glucose OR random blood sugar) AND (prevention OR management OR intervention OR exercise OR physical activity OR diet OR nutrition OR lifestyle) AND (Latina OR Latino OR Hispanic OR Mexican OR Spanish speaking OR Latin American OR Chicano).

Relevant systematic reviews were identified in the PubMed and CENTRAL databases. The abstracts of studies included in these reviews were screened to evaluate if these studies were suitable for inclusion in this review.

Article titles and abstracts were screened for relevance and inclusion. Full text articles were read when needed to determine if the population included at least 50% Latinos or stratified results for race/ethnicity. Eligible full text articles were then read and included in the qualitative review if they met the outcome, intervention, and population criteria.

Outcomes. For studies on the prevention of GDM, the primary outcome was risk of gestational diabetes mellitus, defined as glucose intolerance with onset during pregnancy (ADA 2014a). Studies were not excluded based on the criteria they used to diagnose GDM (3-hour oral glucose tolerance test, etc.), but the diagnostic criteria were carefully noted for each study and considered in the analysis and interpretation of the meta-analysis results. Abnormal glucose tolerance (AGT), defined as a failed 1-hour non-fasting oral glucose challenge test, was also included because it is part of the spectrum of abnormal hyperglycemia in pregnancy, has a defined cutoff value, and is part of the screening process for GDM (ADA 2014a). Secondary outcomes were divided into perinatal maternal and fetal/neonatal outcomes.

Maternal outcomes included mode of birth (cesarean delivery, normal or operative vaginal delivery), hypertensive disorders of pregnancy, and maternal blood glucose control (hemoglobin A1c, fasting blood glucose, random blood glucose). Fetal/neonatal outcomes included perinatal mortality, the incidence of macrosomia, large-for-gestational age, small-for-gestational age, preterm birth, shoulder dystocia, neonatal hypoglycemia, APGAR score, and NICU admission. These outcomes served as the primary outcomes of interest for studies on GDM management.

Data extraction and management. References for all studies returned in the database searches were imported into a reference database in RefWorks.com. Data extraction forms were made in Excel (Microsoft Office 2010™) to collect pre-defined relevant information from the studies for analysis.

Quality assessment. Risk of bias in the included studies was not assessed using the standard criteria proposed by the Cochrane Collaboration because the majority of studies in this review were not randomized controlled trials.[70] Instead, assessment of methodological quality was based upon characteristics deemed most relevant for studies of lifestyle interventions for the prevention and management of GDM. Each article was assessed for the following criteria:

-Study design: Interventional studies with control groups were considered higher quality than a pre-post design. Observational studies controlled for covariates in statistical analyses.

-Defined GDM/AGT and reported GDM/AGT diagnostic criteria.

-Reported low attrition (20% or less lost to follow-up) or compared characteristics between study completers and non-completers.

-Quantified the exposure (lifestyle habits or intervention) in some way that was measurable and reproducible.

-Measured exposure or adherence to lifestyle intervention, even if by self-reported measures.

A study was assigned one point for each criterion that it met and zero points for each criterion that it did not meet. The overall score could range from 0 - 5, meaning that a study of the highest quality by these standards would receive a score of five. Studies meeting four or more of these criteria were

considered good quality, while studies meeting three or fewer of these criteria were considered poor quality.

Data analysis. Meta-analysis was carried out using Mix Pro 2.0 add-in for Excel (©BIOSTAXL 2014). Data from the included studies was copied into Excel and the synthesis forest plot function of Mix Pro 2.0 was used to calculate summary odds ratios and create forest plots based on a fixed effects model. Due to the heterogeneity of interventions and outcomes for which data was reported, meta-analysis was only carried out for the risk of GDM and AGT. In both included studies, Chasan-Taber et al. looked at multiple categories of physical activity, ranging from household/caregiving activities to vigorous or moderate intensity exercise (Chasan-Taber 2008; Chasan-Taber 2014b). Total physical activity was chosen for this meta-analysis due to the assumption that if there is a certain level or intensity of exercise that lowers the risk of GDM, any additional amount of exercise would not likely take away from that effect. The authors of the studies divided women into quartiles or tertiles of physical activity during pre-pregnancy, early pregnancy, and mid-pregnancy. They compared each quartile or tertile to the lowest level group of physical activity, which served as the referent group. The odds ratios for the highest compared to lowest physical activity level groups were used for this meta-analysis. No analysis of publication bias was performed due to the small number of studies included in this review. Cochran's Q statistic of heterogeneity was calculated using the heterogeneity function of Mix Pro 2.0 add-on for Excel.

Ethical considerations. This review was excluded from IRB review because it involved neither data collection from human subjects nor identifiable private information. Since a systematic literature review draws upon the already de-identified data of published studies, Emory IRB approval was not required (Emory IRB 2014). No additional, unpublished data was retrieved in order to perform this meta-analysis.

Limitations. Some of the strengths of a systematic review and meta-analysis are that it combines data from multiple studies, which increases the power to detect a significant treatment effect, and improves precision when estimating the effect of an intervention. It also reduces subjectivity in study selection. However, meta-analyses are limited by heterogeneity amongst their included studies (Higgins

and Green 2011). The broad inclusion criteria of this systematic review allow for some heterogeneity in the interventions (diet, exercise, or both), participants (women without vs. with GDM), and outcomes (choice of outcome indicators and how these are measured). The inclusion criteria were meant to broaden the search, because it was expected that there would be few studies focused on Latina populations. Studies on both prevention and management of GDM were included because there is overlap in their interventions and outcomes. The inclusion criteria allowed for other study designs besides randomized controlled trials to be eligible for this review. Non-randomized studies may introduce confounding and selection bias. Diet and exercise interventions, unless directly observed, may be associated with information bias. Measurement of adherence to diet or exercise by self-report may lead to misclassification of exposure. These expected limitations informed the assessment of methodological quality of the included studies.

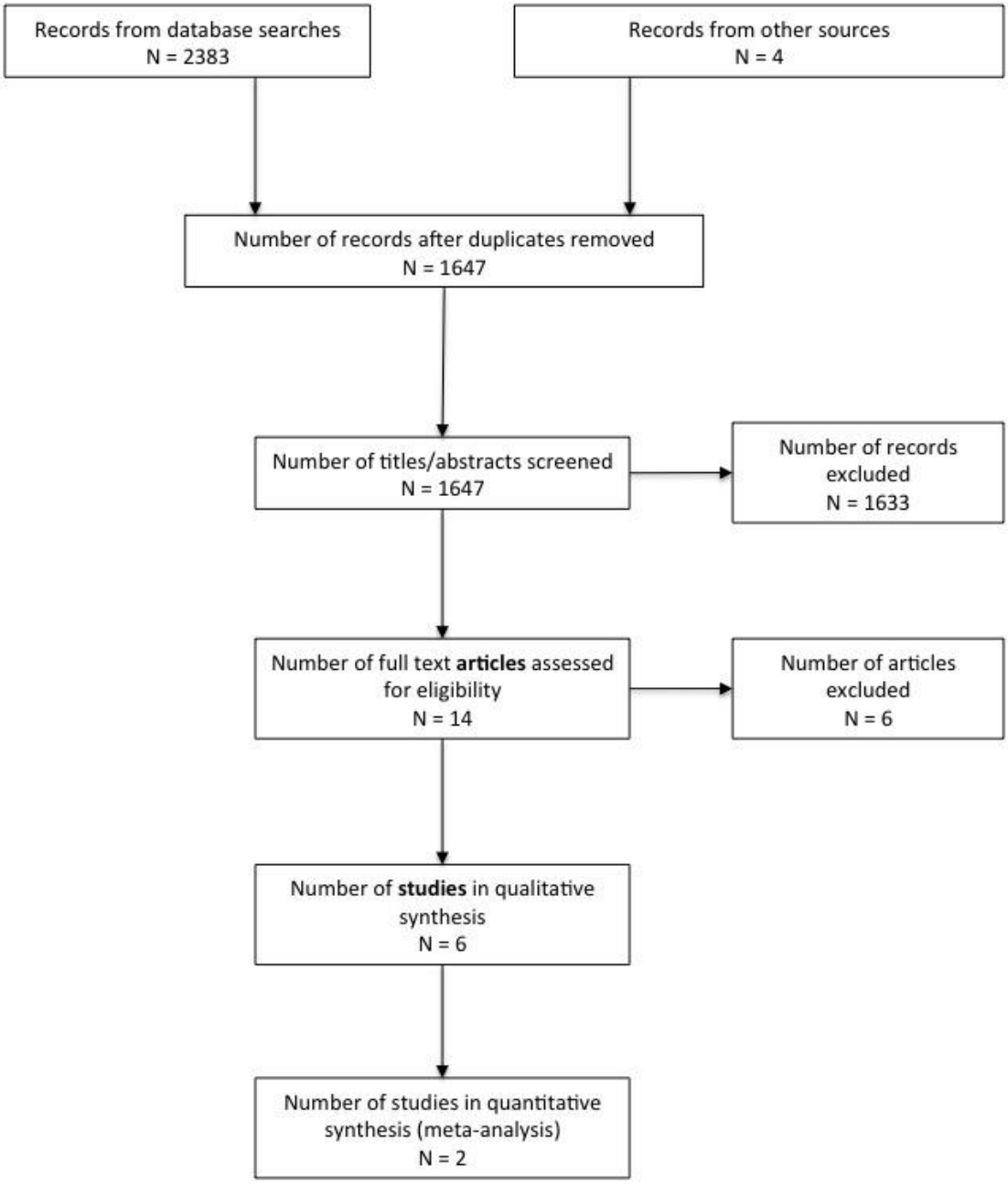
3.2 Results

Selection of studies. The literature search returned 1647 potentially relevant articles. Fourteen were identified as potential articles for inclusion and the full text articles were read to assess eligibility. Six articles were excluded based on exclusion criteria. Three of these articles did not report any outcomes of interest, and three articles did not report data for GDM. Another article was identified from the references of a systematic review on GDM, however, it was not accessible in time for inclusion in this review. Eight articles met the inclusion criteria, one of which was identified through checking references from another systematic review on GDM prevention. Two of the included articles were based off of data from the Latina Gestational Diabetes Study cohort (Chasan-Taber 2008), so there were six individual studies included in this review, with a total of 3101 women. Three of the studies evaluated the risk of developing GDM and three of the studies evaluated the risk of other perinatal outcomes in women already diagnosed with GDM. The tables in Appendices A and B show key characteristics of each article.

Incidence of GDM. The incidence of GDM in these studies ranged from 3.3% to 10.6%, which is consistent with prior findings in this population (Chasan-Taber 2014; Perichart-Perera 2009). Of note, the

study group with the highest incidence of GDM (10.6%) was a population of women in Mexico, which is a country noted to have a particularly high prevalence of GDM (Perichart-Perera 2009). The predominantly Puerto Rican population of women in Massachusetts studied by Chasan-Taber et al. had lower incidences of GDM at 3.3% and 4.6% among the two cohorts (Chasan-Taber 2008; Chasan-Taber 2014b, respectively).

Figure 1: Flow diagram of the study selection process.



3.21 Main Findings

Prevention of GDM

Physical activity. Two studies looked at physical activity at different time periods around pregnancy and the risk of GDM. These two cohorts of pregnant Latinas in Western Massachusetts provided data on a total of 2247 women by prospectively collecting women's self-reported levels of household/caregiving, occupational, active living (walking, bicycling, running errands, etc.), sports/exercise activities, and moderate/vigorous intensity activities. There were no statistically significant associations between the risk of GDM and total physical activity in pre-, early, or mid-pregnancy. The pooled odds ratios suggest that the effect of physical activity may be to lower the risk of GDM, however, the findings did not reach statistical significance [Figures 2-4]. Likewise, there were no statistically significant associations between total physical activity in pre-, early, or mid-pregnancy and the risk of AGT (Chasan-Taber 2008; Chasan-Taber 2014b).

Cochran's Q statistic for pre-, early, and mid-pregnancy was not statistically significant, however, Q has low power to detect heterogeneity with only two studies (Higgins and Green 2011). Although not statistically significant, the I^2 statistic for mid-pregnancy was 40.14%, suggesting the studies may have had heterogeneity in their assessments of mid-pregnancy physical activity and GDM risk.

Diet. There was only one study that evaluated the effect of a dietary intervention on the risk of GDM (Reyes 2012). In the study by Reyes et al., obese and overweight women underwent a medical nutrition program, which consisted of enhanced education about the risks of excessive pregnancy weight gain, and individualized nutritional counseling based on American Dietetic Association recommendations for women with GDM. Normal weight women served as the control group and received no intervention. The study found that even though obese and overweight women underwent a medical nutrition program during pregnancy, obese women retained greater odds of developing GDM compared to normal weight women who underwent no intervention (OR 4.2, 95% CI 1.9-9.3) (Reyes 2012).

Figures 2-4: Forest plots of total pre-, early, and mid-pregnancy physical activity and the risk of GDM.

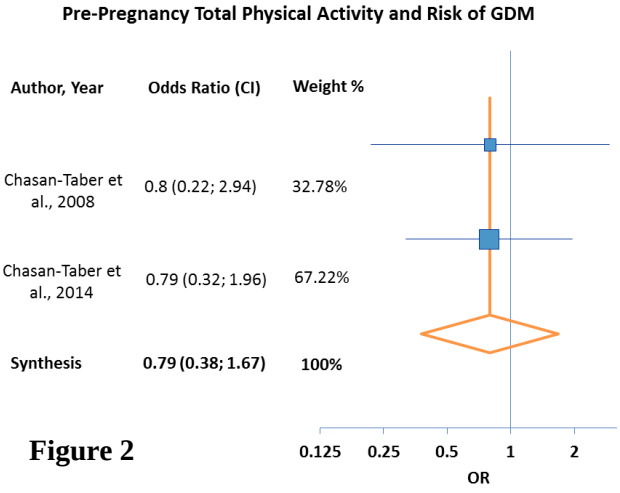


Figure 2

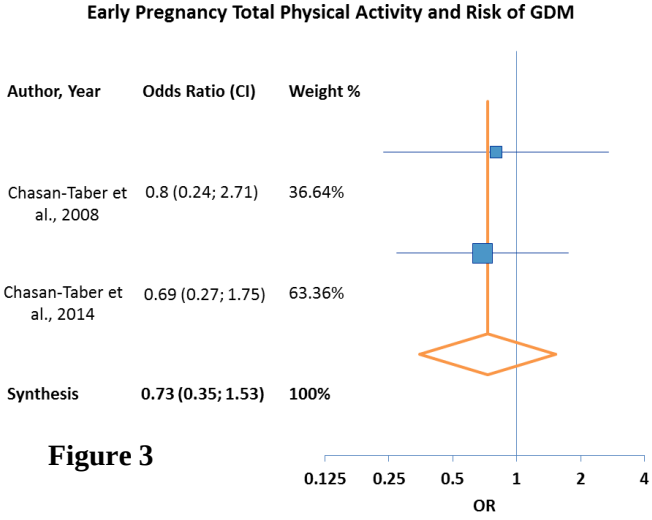


Figure 3

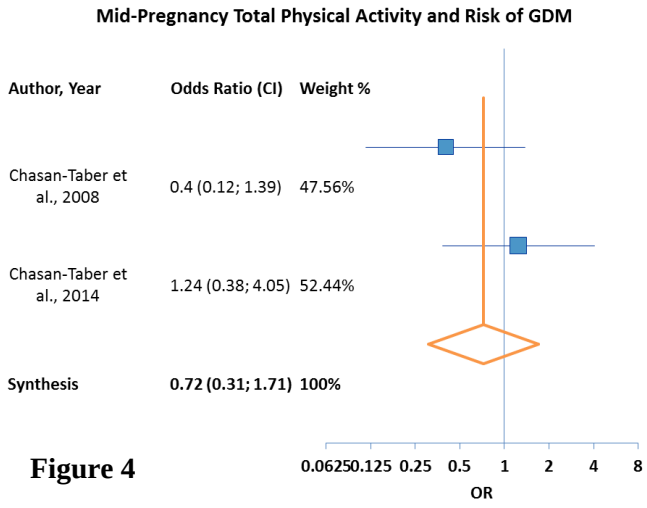


Figure 4

Tovar et al. looked at the effect of specific dietary exposures and the risk of AGT. They did not report data for GDM. In their observational study, they found that women who reported a higher intake of fiber or a higher ratio of polyunsaturated:unsaturated fats had a lower odds of AGT compared to women who reported lower intakes of such diets (OR 0.9, 95% CI 0.84-0.99 and OR 0.1, 95% CI 0.02-0.45, respectively). Likewise, women who reported higher intake of saturated fat compared to lower intake of saturated fat had greater odds of AGT (OR 1.3, 95% CI 1.1-1.5). Compared to women who ate an average amount of energy-dense snack foods, women who ate a low amount of energy-dense snack foods had lower odds of AGT (OR 0.4, 95% CI 0.1-1.0). Tovar et al. found no statistically significant association

between glycemic load or daily fruit/vegetable intake and the risk of AGT (Tovar 2009). A meta-analysis comparing these two studies could not be performed because they reported different primary outcomes (GDM vs. AGT).

Other Perinatal Outcomes

Three of the studies included in this review investigated the effect of lifestyle interventions in Latinas with GDM and the risk of various perinatal outcomes. Macrosomia was the only outcome for which data was available for all three studies. Comparisons of data from Reyes et al. were not possible due to the study's methodology, in which BMI was a confounder in the relationship between the intervention and the risk of GDM.

Macrosomia. Two studies investigated the effect of dietary counseling in women with GDM on the risk of macrosomia (Perichart-Perera 2009; Mendelson 2008). In both studies, there was no statistically significant relationship between dietary counseling and the risk of macrosomia. No meta-analysis was performed on nutritional counseling and macrosomia risk because the definition of macrosomia differed between the two studies. In Perichart-Perera et al., macrosomia was defined as birth weight >4000 grams (Perichart-Perera 2009). In Mendelson et al., macrosomia was defined as a weight:length ratio greater than the 90th percentile for gestational age (Mendelson 2008). In the quasi-experimental study by Perichart-Perera et al., women in the intervention group received individual nutritional counseling and intensive education from a clinical dietitian. Nutrition recommendations were based on GDM management guidelines from the American Dietetic Association (Perichart-Perera 2009). In the randomized controlled trial by Mendelson et al., women randomized to the Parish Nurse Intervention Program participated in counseling sessions that taught nutritional recommendations for management of GDM based on the California Diabetes and Pregnancy Program Sweet Success guidelines. The Parish Nurse intervention also included a component of spiritual encouragement (Mendelson 2008).

Bung et al. also looked at the risk of macrosomia for women with GDM, however, the intervention in this study was exercise-based and consisted of thrice weekly exercise sessions on

recumbent bicycles at 50% of the women's aerobic exercise capacities. Women in the exercise group also received standard dietary recommendations and insulin as needed to manage hyperglycemia. Women in the control group received only the standard dietary recommendations and insulin therapy; they did not undergo the exercise program. In this study, there was no statistically significant difference in the risk of macrosomia between the intervention and control groups (Bung 1991).

Preeclampsia. Two studies reported data for hypertensive disorders of pregnancy. Perichart-Perera observed a lower risk of preeclampsia among type 2 diabetic women who received medical nutritional therapy compared to the control group, but did not observe a statistically significant association between medical nutrition therapy and the risk of preeclampsia for women with GDM (Perichart-Perera 2009). Reyes et al. found that despite receiving medical nutrition therapy, obese women had an elevated odds of developing preeclampsia compared to normal weight women (OR 3.3, 95% CI 1.2-8.8) (Reyes 2012). These studies were not compared in a meta-analysis due to the heterogeneity of the interventions.

Cesarean delivery. Two studies reported data for the risk of cesarean deliveries among women with GDM. Bung et al. found that as with macrosomia, there was no statistically significant difference in the odds of having a cesarean delivery for the exercise and diet group compared to the insulin and diet group (Bung 1991). Reyes et al. found that obese women, despite undergoing medical nutrition therapy, were more likely to have a planned cesarean delivery compared to both normal weight ($p<0.0001$) and overweight ($p<0.05$) women (Reyes 2012).

Preterm delivery. Perichart-Perera et al. and Reyes et al. provided data on preterm deliveries among women with GDM. Both studies defined preterm as being born at less than 37 weeks gestation. Perichart-Perera et al. found no statistically significant relationship between the medical nutrition intervention and the risk of preterm birth (Perichart-Perera 2009). In their retrospective study of medical nutrition therapy for obese/overweight women, Reyes et al. found no statistically significant difference in the odds of preterm delivery for obese or overweight women in the intervention group compared to normal weight women in the control group (Reyes 2012).

3.22 Methodological Quality

Based on the methodological quality criteria used in this review, four of the six studies were considered good quality. Table 1 shows the results in greater detail. The study by Reyes et al. was considered low quality because it did not report whether covariates were controlled for in statistical analyses and did not measure participant adherence to nutrition recommendations, although the latter was a limitation of the study's retrospective cohort design (Reyes 2012). The randomized controlled trial performed by Mendelson et al. was also considered low quality because it did not report the criteria used to diagnose women with GDM and did not measure adherence to the lifestyle recommendations of the intervention (Mendelson 2008).

Table 1: Methodological quality of the included studies.

Study	Study Design	Defined GDM or AGT	Attrition	Quantified Exposure	Measured Adherence/ Exposure	**Total Score**
Chasan-Taber et al. 2008	1	1	1	0	1	**4**
Chasan-Taber et al. 2014	1	1	1	1	1	**5**
Reyes et al. 2012	0	1	1	1	0	**3**
Bung et al. 1991	1	0	1	1	1	**4**
Mendelson et al. 2008	1	0	1	1	0	**3**
Perichart-Perera et al. 2009	1	1	1	1	1	**5**

Chapter 4: Discussion, Recommendations, and Conclusion

4.1 Discussion

This systematic literature review identified six original studies that met the inclusion criteria, only three of which provided data on GDM as a primary outcome (Chasan-Taber 2008; Chasan-Taber 2014b; Reyes 2013). The remaining three studies investigated lifestyle interventions for the prevention of adverse perinatal outcomes associated with GDM (Perichart-Perera 2009; Mendelson 2008; Bung 1991). In the meta-analysis of 2,247 women from two observational studies, there was no statistically significant relationship between total physical activity in pre-, early, or mid-pregnancy and the risk of GDM. Meta-analysis could only be performed for the relationship between physical activity and risk of GDM, so evidence for other types of lifestyle interventions or other perinatal outcomes is limited to what is reported in single studies.

4.11 Prevention of GDM

Physical activity. The pooled odds ratios for total physical activity and GDM risk from this meta-analysis suggest that higher physical activity levels may lower the risk of developing GDM, however, these results were not statistically significant [Figures 2-4]. Despite the relatively large sample size, the prevalence of GDM was low and the studies may not have been powered to detect a difference in the risk of GDM when the samples were divided into quartiles (Chasan-Taber 2008; Chasan-Taber 2014b). Additionally, both of the studies by Chasan-Taber et al. were observational and the highest physical activity groups may not have achieved high enough levels of exercise to impact the risk of GDM. The amount of physical activity was not well quantified in the 2008 study by Chasan-Taber et al. For example, the highest physical activity frequency in the study was classified as “always or more than once a week” (Chasan-Taber 2008). Women often decrease their physical activity levels throughout pregnancy and Latinas tend to report having lower than average exercise levels during pregnancy (Chasan-Taber 2014b; Chu 2009; Petersen 2005). Although the reason for this is unclear, one qualitative study identified that Latinas, more so than non-Hispanic white women, reported lack of energy and information about suitable exercises during pregnancy as barriers to exercise during pregnancy (Marquez 2009). Consistent

with this trend, Chasan-Taber et al. observed a decrease in vigorous intensity activity towards mid-pregnancy, a time when women are screened for GDM (ADA 2014a) and when exercise may have the most impact on the risk of GDM (Chasan-Taber 2008).

The results of this meta-analysis differ from that of a previous meta-analysis of physical activity and GDM risk, in which those authors found that higher total physical activity during pre-pregnancy and early pregnancy reduced the risk of GDM compared to lower total physical activity (pooled OR 0.45, 95% CI 0.28-0.75). That meta-analysis included a larger sample size of 34,000 women from eight studies, and included predominantly non-Hispanic white women (Tobias 2011). Similar to this review, it included no randomized controlled trials, which are traditionally considered the gold standard of research design for interventional studies (Higgins and Green 2011). One meta-analysis that did include randomized controlled trials found no statistically significant relationship between physical activity and the incidence of GDM or insulin sensitivity. However, that meta-analysis consisted of a smaller sample size (1,115 women) and included no studies with Latina women (Han 2012). The evidence on this topic is conflicting, and more large-scale randomized controlled trials are needed before making recommendations for exercise in pregnancy to prevent GDM.

One possible explanation for the difference in results of this meta-analysis and that of Tobias et al. is that the activities found by Tobias et al. to significantly reduce GDM risk (brisk walking, stair climbing, and vigorous activity) may be more vigorous than the activities measured in the studies included in this meta-analysis (Tobias 2011). Several studies have shown a significant difference in glucose tolerance and insulin sensitivity for women undergoing exercise interventions in pregnancy compared to control groups, however, these same studies failed to show a significant difference in the incidence of GDM between groups (Ruchat and Mottola 2013). Based on these studies, it seems that exercise affects glycemia, but higher levels of exercise may be needed to affect the risk of GDM. In the Latina Gestational Diabetes Mellitus Study cohort, Chasan-Taber et al. found a lower risk of GDM with higher mid-pregnancy sports/exercise. Sports/exercise is likely to be more vigorous than the other physical activity categories in the study. Chasan-Taber et al. also found a decreased risk of GDM for

women in the highest levels of household/caregiving activity in pre- and mid-pregnancy, which would not seem to fit with this explanation, but once again is limited by the study's measurement exposure tool (Chasan-Taber 2008).

The timing of the effect of sports/exercise in mid-pregnancy makes sense in light of the fast onset and offset of insulin sensitivity after exercise and the time at which GDM is diagnosed (mid-pregnancy) (Artal 2014). The same association was not observed in the second study by Chasan-Taber et al., but may be due to the fact that vigorous activity and sports/exercise activity decreased by mid-pregnancy in this cohort (Chasan-Taber 2014b). The normal course of pregnancy leads to maternal insulin resistance around gestational weeks 24 to 28 in order to divert glucose to the growing fetus (Tobias 2011). Women who develop GDM seem to have an underlying pancreatic beta-cell dysfunction and less insulin secretion than women who do not develop GDM. Prior diabetes prevention studies have shown that lifestyle interventions and treatment of insulin resistance can help preserve beta-cell function (Metzger 2007). Lifestyle interventions may also be useful for prevention of GDM, but the nature of pregnancy limits the timing and intensity of eligible interventions. Given that underlying beta-cell dysfunction seems to predate pregnancy, it may be that no amount of diet or exercise during pregnancy can make up for this predisposition. However, if the dysfunction can be alleviated with diet and exercise, these interventions may need to be continued throughout pregnancy to suppress progression of beta-cell dysfunction. This would explain the lack of effect of total physical activity on GDM risk, as physical activity decreased during the course of pregnancy in both studies of this meta-analysis (Chasan-Taber 2008; Chasan-Taber 2014b).

Diet. More studies of specific dietary interventions for the prevention of GDM are needed, as evidenced by the fact that this review identified only one study that looked at the relationship of diet and GDM among Latinas. Two of the dietary studies included in this review utilized medical nutrition programs based on the recommendations of the American Dietetic Association. The recommendations are multi-faceted, and include restriction of carbohydrates to 40-45% of total calories, calorie restriction for obese women, and specific weight gain recommendations (Lindell and Quintana 2011). None of the

studies in this review compared a low glycemic index diet to the risk of GDM or its associated perinatal outcomes. Previous studies suggest that low glycemic index diets may reduce the need for insulin in the management of GDM, but there is a need for larger, well-designed studies on this topic (Tieu 2011; Vercoza Viana 2014).

The relationship between medical nutrition therapy and GDM risk could not be clearly defined in the study by Reyes et al. because it was confounded by obesity – a limitation of the study design. However, the study showed that obesity is such a potent risk factor for GDM and its associated health outcomes that a medical nutrition intervention could not overcome the effect of BMI on the risk of GDM. In fact, obese women retained a four-fold higher odds of developing GDM compared to normal weight women (Reyes 2012). This is important to keep in mind when designing future studies and intervention programs, because overweight/obese women may need to focus primarily on weight loss or limiting weight gain.

One study compared specific dietary exposures with the risk of abnormal glucose tolerance (Tovar 2009). Although AGT is not equivalent to GDM, it may be similar in its relationship to perinatal outcomes and development of type 2 diabetes, since there is a direct relationship between increasing glucose levels in pregnancy and the risk of adverse perinatal outcomes (Coustan 2010). Similar to studies of diet and GDM risk, the study by Tovar et al. found a higher risk of AGT with higher saturated fat intake and with lower fiber intake (Bo 2001; Zhang 2006). Tovar et al. also observed a lower risk of AGT with lower intake of energy dense snack foods; this risk was 60% lower for women who consumed less than 400 kcals of such snack foods per day (95% CI 0.1 - 1). Unlike findings from prior studies of GDM, lower dietary glycemic load was not associated with a lower risk of developing AGT (Vercoza Viana 2014; Tovar 2009). However, this is a single study whose primary outcome was AGT rather than GDM and cannot be directly compared to these studies.

4.12 Prevention of Other Perinatal Outcomes

Macrosomia. In both nutritional studies, there was no significant relationship between nutritional counseling among women with GDM and the rate of macrosomia (Perichart-Perera 2009; Mendelson

2008). These studies relied upon self-report and participant recall to measure adherence with the intervention, which could lead to misclassification of exposure. In the exercise study by Bung et al., none of the women in the exercise and diet group required insulin and there was no significant difference in the rate of macrosomia compared to the control group (insulin and diet), suggesting that exercise for women with GDM may be as effective as insulin at controlling blood glucose levels and the risk of macrosomia. However, this study had a small sample size with only 6 cases of macrosomia. The level of exercise was more intense than in other studies, and achieved perhaps unrealistic adherence to the intervention by requiring women to exercise under observation in a lab. For ethical reasons, there was no comparison group that did not receive an intervention and it cannot be determined if exercise or insulin would reduce the risk of macrosomia compared to no treatment (Bung 1991). Prior studies support the protective effect of insulin treatment in women with GDM on the risk of macrosomia (Coustan 1984; Turok 2003) and the type of intervention (insulin, diet, or exercise) may be less important than the degree of glycemic control achieved (Langer 1988).

Preeclampsia, cesarean delivery, and preterm delivery. None of the studies included in this review identified a statistically significant protective effect of physical activity or diet on the incidence of preeclampsia, cesarean deliveries, or preterm deliveries. In fact in one study, despite undergoing medical nutrition therapy, obese women had a greater odds of preeclampsia and planned cesarean sections compared to normal weight women who did not receive medical nutrition therapy (Reyes 2012). This study highlights the potent effect of obesity and overweight on several perinatal outcomes. In the other studies of lifestyle interventions for management of GDM, lack of effect of interventions may be due to insufficient levels of exercise and diet. Lifestyle interventions are bound to face challenges with compliance, and two of the GDM management studies in this review either relied upon participant self-report of adherence or did not measure adherence to the intervention (Perichart-Perera 2009; Mendelson 2008).

4.13 Strengths and Weaknesses

This systematic literature review and meta-analysis has several limitations. The criterion for inclusion of Latinas significantly reduced the number of studies eligible for inclusion in the review. This excluded many studies on the topic that did not include Latinas, but the results of which may be equally applicable to Latinas. However, this systematic review aims to identify research specific to Latinas in order to help fill a gap in knowledge about a population with an overall elevated risk of GDM. Since there are so few studies of GDM in Latinas, the scope of the review was widened to include study designs that are less rigorous than randomized controlled trials. The two studies included in the meta-analysis of GDM risk were observational and non-randomized. Because they were not randomized, there is a possibility that women with the highest levels of physical activity may have been inherently different in some way from women in the lowest levels of physical activity that was not accounted for in statistical analyses. For example, women who achieve higher levels of physical activity may be generally healthier or more likely to have other beneficial behaviors compared to less physically active women.

The inclusion criteria used in the search strategy allowed studies to define GDM by different diagnostic criteria, which could introduce heterogeneity in measurement of the primary outcome of this review. Fortunately, all three studies of GDM prevention used the same American Diabetes Association diagnostic criteria published in 2004. GDM was diagnosed with a two-step process, if a woman had at least two of the following blood glucose values after a 100 gram fasting oral glucose tolerance test: fasting $\geq$ 95 mg/dL, 1 hour $\geq$ 180 mg/dL, 2 hours $\geq$ 155 mg/dL, 3 hours $\geq$ 140 mg/dL (ADA 2014a). In their 2008 study, Chasan-Taber et al. used additional diagnostic criteria that may have increased their sensitivity to detect GDM (Chasan-Taber 2008). Perichart-Perera et al. also used the 2004 ADA diagnostic criteria for GDM (Perichart-Perera 2009). Both Bung et al. and Mendelson et al. reported women being diagnosed with GDM by physicians prior to entry into their studies, but did not report the specific criteria by which women were diagnosed with GDM (Bung 1991; Mendelson 2008). Misclassification of GDM status may have occurred as a result.

The observational nature of the studies in the meta-analysis is not ideal for identifying effective GDM prevention interventions. It is possible that the maximum physical activity levels achieved by women in the studies was below levels that affect the development of GDM, since physical activity tends to decrease during pregnancy and Latinas are less likely to meet exercise guidelines for pregnancy compared to non-Hispanic white women (Chasan-Taber 2014a; Chu 2009; Petersen 2005). In the 2008 study by Chasan-Taber et al., the questionnaire only categorized physical activity up to "more than once a week" (Chasan-Taber 2008). The American College of Obstetricians and Gynecologists (ACOG) recommend that all pregnant women exercise for at least 30 minutes on most days of the week (Artal 2003). The benefit of increased insulin sensitivity associated with exercise may decrease within 48 hours, so the frequency of exercise is important to maintain its benefits (Artal 2014). However, in their second study, Chasan-Taber et al. found no significant relationship between meeting ACOG guidelines for exercise in pregnancy and the risk of GDM. A caveat of this study is that physical activity was quantified based on the activities that women self-reported for time periods as far back as a year prior to the study (Chasan-Taber 2014b). Therefore it is possible that women with the highest self-reported level of physical activity may have actually had less physical activity than what is recommended or effective at preventing GDM. Despite the drawbacks of the observational study design, these studies provide data on the actual physical activity behaviors of Latinas during pregnancy and provide a frame of reference for the feasibility of physical activity interventions in this population.

Most of the studies utilized self-report or did not measure adherence to the intervention. They were also unable to obtain sufficient objective physiological data such as blood glucose or insulin levels. It is likely that participants in the studies may not have been as compliant with the recommended diet and exercise as they reported. Studies of the validity of self-report for assessing physical activity suggest that self-report does not accurately estimate physical activity, and that estimates based on self-report may be higher or lower than actual physical activity. The unpredictability of under- or over-estimation of physical activity makes it difficult to correct for self-report bias (Prince 2008).

Another limitation of this review is that all of the included studies recruited women from medical clinics, and generalizability of results beyond these studies is limited because not all women receive prenatal care. Approximately 32% of Hispanic women do not initiate prenatal care in the first trimester (Office on Women's Health 2013). Women who do not receive prenatal care or who only receive care at the end of pregnancy may differ in many ways from women who do receive prenatal care. Additionally, the effectiveness of lifestyle interventions may differ between women who do and do not receive prenatal care because healthcare professionals can provide behavioral reinforcement and encouragement at regular intervals.

Three of the studies noted statistically significant baseline differences between women with missing data and those included in analysis, which may introduce selection bias and confounding. Women who did not complete the mid-pregnancy interview were significantly more likely to have higher education, higher income, and more preterm births (Chasan-Taber 2008). Tovar et al. observed a similar occurrence in which women missing the relevant data were more likely to be older and multiparous compared to women with data for analysis (Tovar 2009). In the second study by Chasan-Taber et al. women with missing data were more likely to prefer to speak English, be highly acculturated, and have a family history of diabetes (Chasan-Taber 2014b). Although Chasan-Taber et al. adjusted for age in their analyses, they did not adjust for socioeconomic factors like income or education due to their sample size (Chasan-Taber 2008). In the study by Reyes et al., normal weight women were younger, more likely to be primigravid, and less likely to have first-degree relatives with diabetes compared to the overweight and obese women. Reyes et al. do not report adjusting for these variables in their analyses (Reyes 2012).

The populations recruited in the studies limit generalizability of the findings in this review. The cohorts studied by Chasan-Taber et al. included mostly young women below the age of 25 years old, which may explain the relatively low prevalence of GDM in these studies. Most of the research on GDM prevention in Latinas has been limited to women of Puerto Rican and Dominican heritage (Chasan-Taber 2008; Chasan-Taber 2014b; Tovar 2009; Fortner 2011; Gollenberg 2010; Gollenberg 2011). Therefore the results of the meta-analysis may not be representative of the effect of physical activity on the risk of

GDM in other Latina subgroups. The difference in predisposition to GDM between subgroups is suggested by the difference in incidence of GDM observed in this review. GDM incidence ranged from 3.3% in the predominantly Puerto Rican cohort studied by Chasan-Taber et al. to 10.6% in the Mexican sample studied by Reyes et al., despite using the same diagnostic criteria (Chasan-Taber 2008; Reyes 2012). This emphasizes the issue of attempting to categorize a diverse group of people as one ethnic category. Until more GDM research includes Latinas, we must use a broader definition for the Latino population in order to draw enough information on the topic. A strength of this review is that it involved a systematic search of scientific literature databases for all published research on GDM prevention and management relevant to Latinas, and confirmed the fact that research is lacking on this topic.

4.2 Recommendations

Perform more research to determine GDM incidence in different populations. In the process of attempting to fill a knowledge gap regarding prevention and management of GDM in Latinas, this review identified that there is insufficient research on this topic. Little GDM research has been done among the minority population groups that are disproportionately affected by GDM. Latinos are the largest ethnic/racial minority population in the U.S., with Mexican Americans comprising the largest subgroup (CDC 2015). Consistent with prior research, this review observed that women of Mexican heritage, especially those living in Mexico, have a higher risk of GDM than other Latino subgroups (Reyes 2012). More population-based research is needed to better describe the difference in risk, in order to begin to understand the factors that put certain women at such elevated risk for GDM and identify points of intervention.

Perform large-scale randomized controlled trials of lifestyle interventions for prevention of GDM and its associated perinatal outcomes among Latinas. Unfortunately, there is insufficient evidence at this time to make recommendations for diet and exercise guidelines for GDM prevention and management in Latinas. Prior meta-analysis of GDM prevention suggest that more total physical activity in pre- and early pregnancy, and a lower glycemic index diet during pregnancy may reduce the risk of developing GDM (Tobias 2011; Vercoza Viana 2014). The studies in this review and meta-analysis did

not find significant associations between these factors, however, the studies may not have accurately measured exposure to diet and exercise due to problems with adherence and participant self-report. There were also few studies examining these relationships in Latinas.

Design future studies with the following recommendations in mind:

1. Future research should build off of the specific interventions found to be beneficial in other studies.
2. Future studies should investigate the effect of specific lifestyle interventions in high-risk Latina populations.
3. Study design should include objective biological outcomes such as blood glucose levels and insulin response, in addition to the incidence of GDM.
4. Future studies should consider other adverse perinatal outcomes associated with GDM, because evidence suggests that levels of glucose intolerance below the diagnostic cutoff for GDM are associated with adverse outcomes (Coustan 2010).
5. Future studies should seek to recruit women who would not normally receive early prenatal care.
6. Future studies should take into consideration the challenges of measuring adherence to lifestyle interventions.
7. Mixed methods studies may prove especially beneficial to elucidate cultural barriers and facilitators to following lifestyle interventions during pregnancy. Studies or programs that include process evaluations or community-based participatory research may provide information for medical and public health providers that could improve the effectiveness of interventions.

Focus public health interventions and policy changes on reducing obesity among women. Although this systematic review and meta-analysis found no significant relationship between diet or exercise exposures and GDM risk, obesity was identified as a strong risk factor for GDM and related perinatal outcomes (Chasan-Taber 2008; Chasan-Taber 2014b; Perichart-Perera 2009; Reyes 2013). The

study by Reyes et al. demonstrated that obesity consistently increased the risk of adverse outcomes for women with GDM compared to normal weight women with GDM. Despite undergoing medical nutrition therapy, obese women had a 4.2 times greater odds of developing GDM compared to normal weight women who did not receive medical nutrition therapy ($p<0.001$). Obese women also had higher odds of preeclampsia (OR 3.3, $p<0.001$) and lack of spontaneous labor (OR 2.4, $p<0.001$) (Reyes 2012). Obesity is also a risk factor for type 2 diabetes mellitus (ADA 2015). Perhaps a more effective, albeit challenging approach to preventing adverse perinatal outcomes is to focus on weight loss for overweight/obese females of childbearing age or younger.

4.3 Conclusion

This systematic review of the literature identified that there is insufficient evidence to recommend specific diet or exercise interventions for the prevention of gestational diabetes mellitus or its related perinatal outcomes in Latinas. The meta-analysis found no significant relationship between exposure to physical activity and the risk of developing GDM. However, only three observational studies of GDM prevention in Latinas were eligible for inclusion in this review, even with relatively broad inclusion criteria. Although not statistically significant, the summary odds ratios obtained in the meta-analysis suggest that the effect of physical activity in pregnancy may be to lower the risk of GDM. Three experimental studies of GDM management in Latinas were included, but heterogeneity in their methodologies prohibited meta-analysis of their data. One of these studies showed similar rates of macrosomic infants born to Latinas with GDM who underwent aerobic exercise during pregnancy compared to Latins with GDM who received insulin (Bung 1991). This was the only experimental study of exercise in pregnancy included in this review and may have been the only study to achieve high enough levels of physical activity to affect the risk of glycemia.

The similarities in pathophysiology of GDM and type 2 diabetes mellitus suggest that lifestyle changes may be beneficial in the prevention and management of GDM, as they are for type 2 diabetes, though pregnancy poses unique challenges and opportunities. More targeted lifestyle interventions may be necessary to prevent GDM and its related adverse perinatal outcomes. Prior meta-analyses of

diet/exercise exposure and GDM risk have conflicting results, although most agree that the quality of existing evidence is low (Han 2012; Han 2013; Oostdam 2011; Tieu 2011). The vast majority of studies on this topic included predominantly non-Hispanic white women and their results have questionable generalizability to other populations. This review highlights the need and the importance of more research on GDM prevention and management in high-risk populations such as Latinas, in hopes that this knowledge will guide interventions that reduce the incidence of gestational diabetes, adverse perinatal outcomes, and subsequent type 2 diabetes mellitus.

References

ADA (2014). Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care, 37(1),* 581-90.

ADA (2014). Standards of Medical Care in Diabetes - 2014. *Diabetes Care, 37(1)*: S14 - S80.

ADA (2015). "Modifiable Risk Factors" and "Non-Modifiable Risk Factors." Retrieved from http://professional.diabetes.org/ResourcesForProfessionals.aspx?cid=60382 and http://professional.diabetes.org/resourcesforprofessionals.aspx?typ=17&cid=60390

AHRQ (2012). Screening and Diagnosing Gestational Diabetes Mellitus. AHRQ Publication No. 12(13): E021-EF.

Artal, R. (2003). Guidelines of the American College of Obstetricians and Gynecologists for exercise during pregnancy and the postpartum period. *Br J Sports Med, 37(1),* 6-12.

Artal, R. (2014). The role of exercise in reducing the risks of gestational diabetes mellitus in obese women. *Best Practice & Research Clinical Obstetrics and Gynaecology, 2014:* 1 - 10. Retrieved from http://dx.doi.org/10.1016/j.bpobgyn.2014.05.013

Baxley, E. and Gobbo, R. (2004). Shoulder Dystocia. *Am Fam Physician, 69(7),* 1707-14. Retrieved from http://www.aafp.org/afp/2004/0401/p1707.html

Benhalima, K. (2014). Screening and management of gestational diabetes. *Best Practice & Research Clinical Obstetrics and Gynaecology, 2014*, 1-11.Bo, S. (2001). Dietary fat and gestational hyperglycaemia. *Diabetologia, 44(8)*: 972 - 8.

Boney, C.M. (2005). Metabolic Syndrome in Childhood: Association With Birth Weight, Maternal Obesity, and Gestational Diabetes Mellitus. *Pediatrics, 115(3),* e290-6.

Bowers, K. (2013). Gestational diabetes, pre-pregnancy obesity and pregnancy weight gain in relation to excess fetal growth: variations by race/ethnicity. *Diabetologia, 56,* 1263-71.

Bryson, C.L. (2003). Association between Gestational Diabetes and Pregnancy-induced Hypertension. *Am J Epidemiol, 58,* 1148–1153.

Bung, P. (1991). Exercise in Gestational Diabetes, An Optional Therapeutic Approach? *Diabetes, 40(2):* 182-5. *JOGNN, 37:* 415-25.

Calderon, J. (1992). Hispanic and Latino: The Viability of Categories for Panethnic Unity. *Latin American Perspectives, 19(4),* 37-44.

CDC (2011). National Diabetes Fact Sheet, 2011. National Center for Chronic Disease Prevention and Health Promotion. Retrieved from http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf

CDC (2014). National Diabetes Statistics Report, 2014. Retrieved from http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf

CDC (2015). "Hispanic or Latino Populations." Retrieved from http://www.cdc.gov/minorityhealth/populations/REMP/hispanic.html

Chasan-Taber, L. (2008). Physical Activity and Gestational Diabetes Mellitus among Hispanic Women. *Journal of Women's Health, 17(6),* 999-1008.

Chasan-Taber, L. (2014). Lifestyle interventions to reduce risk of diabetes among women with prior gestational diabetes mellitus. *Best Practice & Research Clinical Obstetrics and Gynaecology, 29(1),* 1-3. Retrieved from http://dx.doi.org/10.1016/j.bpobgyn.2014.04.019

Chasan-Taber, L. (2014). Physical activity before and during pregnancy and risk of abnormal glucose tolerance among Hispanic women. *Diabetes and Metabolism, 40*: 67 - 75.

Chatfield, J. (2001). Practice Guidelines: ACOG Issues Guidelines on Fetal Macrosomia. *Am Fam Physician, 64(1),* 169-170. Retrieved from http://www.aafp.org/afp/2001/0701/p169.html

Chen, Y (2009). Cost of Gestational Diabetes Mellitus in the United States in 2007. *Population Health Management, 12(3):* 1-10.

Chu, S. (2009). Gestational weight gain by body mass index among US women delivering live births, 2004-2005: fueling future obesity. *Am J Obstet Gynecol, 200,* 271.e1-271.e7.

Cosgrove, P. (2002). Cost-effective approaches to diabetes care and prevention. *Diabetes Voice, 47(4),* 13-6.

Coustan, D. (1984). Prophylactic insulin treatment of gestational diabetes reduces the incidence of macrosomia, operative delivery, and birth trauma. *AJOG, 150(7):* 836-42.

Coustan, D. (2010). The HAPO Study: Paving The Way For New Diagnostic Criteria For GDM. *Am J Obstet Gynecol., 202(6),* 654.e1–654.e6.

Coustan, D. (2014). Diabetes mellitus in pregnancy: Screening and diagnosis. UpToDate. Retrieved from http://www.uptodate.com/contents/diabetes-mellitus-in-pregnancy-screening-and-diagnosis

Coustan, D. (2015). Gestational diabetes mellitus: Glycemic control and maternal prognosis. UpToDate. Retrieved from http://www.uptodate.com/contents/gestational-diabetes-mellitus-glycemic-control-and-maternal-prognosis

Crume, T.L. (2011). Association of exposure to diabetes in utero with adiposity and fat distribution in a multiethnic population of youth: the Exploring Perinatal Outcomes among Children Study. *Diabetologia, 54(1),* 87-92.

Dabelea, D. (2005). Increasing Prevalence of Gestational Diabetes Mellitus (GDM) Over Time and by Birth Cohort. *Diabetes Care, 28(3),* 579-84.

Davis, J. (2013). The impact of gestational diabetes mellitus on pubertal changes in adiposity and metabolic profiles in Latino offspring. *J Pediatr, 162(4),* 741-5.

Declercq, E. (2007). Maternal Outcomes Associated With Planned Primary Cesarean Births Compared With Planned Vaginal Births. *Obstetrics & Gynecology, 109(3),* 669-77.

Emory IRB (2014). "Not Human Subjects." Retrieved from http://www.irb.emory.edu/policies/review-types/not-human.html

Ferrari, R. (2013). A qualitative study of women's perceptions of provider advice about diet and physical activity during pregnancy. *Patient Educ Couns, 91(3),* 372–77.

Fortner, R. (2011). Physical Activity and Hypertensive Disorders of Pregnancy among Hispanic Women. Medicine & Science in Sports & Exercise, 2011: 639 - 46. doi: 10.1249/MSS.0b013e3181f58d3e

Fujimoto, W. (2013). Gestational Diabetes in High-Risk Populations. *Clinical Diabetes, 31(2),* 90-4.

Gollenberg, A. (2010). Sedentary Behaviors and Abnormal Glucose Tolerance among Pregnant Latina Women. *Journal of the American College of Sports Medicine.* DOI: 10.1249/MSS.0b013e3181c6dec8. Pp 1079-85.

Gollenberg, A. (2011). Physical Activity and Risk of Small-for-Gestational-Age Birth Among Predominantly Puerto Rican Women. *Matern Child Health J, 15:* 49–59.

Han, S. (2012). Exercise for pregnant women for preventing gestational diabetes mellitus. *Cochrane Database of Systematic Reviews 2012, 7, 1-48. doi:*10.1002/14651858.CD009021.pub2

Han, S. (2013). Different types of dietary advice for women with gestational diabetes mellitus. *Cochrane Database of Systematic Reviews 2013, 3,* 1-76. doi:10.1002/14651858.CD009275.pub2

Hawkins, M. (2014). A pregnancy lifestyle intervention to prevent gestational diabetes risk factors in overweight Hispanic women: a feasibility randomized controlled trial. *Diabetic Medicine*. doi: 10.1111/dme.12601

Higgins J.P.T., Green S., editors. (2011). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Retrieved from www.cochrane-handbook.org

Holub, C. (2013). Obesity Control in Latin American and U.S. Latinos. *Am J Prev Med, 44(5),* 529-37.

Jovanovic, L. (2004). Gestational Diabetes Mellitus. *JAMA, 286(20),* 2516-8.

Kieffer, E. (2006). The Influence of Maternal Weight and Glucose Tolerance on Infant Birthweight in Latino Mother–Infant Pairs. *American Journal of Public Health, 96(12),* 2201-8.

Kim, C. (2002). Gestational Diabetes and the Incidence of Type 2 Diabetes. *Diabetes Care, 25(10):* 1862-8.

Kjos, S.L. (1995). Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum glucose tolerance testing. *Diabetes, 44(5),* 586-91.

Knowler, W. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med, 346(6),* 393-403.

Kolas, T. (2006). Planned cesarean versus planned vaginal delivery term: Comparison of newborn infant outcomes. *American Journal of Obstetrics and Gynecology,195:* 1538–43.

Langer, O. (1988). The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. *AJOG, 159(6):* 1478-83.

Lindell, A., and Quintana, L. (2011). "Gestational Diabetes Mellitus: Incorporating the New Dietary Guidelines." *On The Cutting Edge, 32(2).* Retrieved from http://www.dce.org/publications/on-the-cutting-edge/incorporating-the-new-dietary-guidelines/

Mandy, G. (2014). Large for gestational age newborn. UpToDate.com. Retrieved from http://www.uptodate.com/contents/large-for-gestational-age-newborn

Marquez, D. (2009). Perspectives of Latina and Non-Latina White Women on Barriers and Facilitators to Exercise in Pregnancy. *Women Health, 49(6),* 505-21.

McDonald, J. (2008). Reproductive Health of the Rapidly Growing Hispanic Population: Data from the Pregnancy Risk Assessment Monitoring System, 2002. *Matern Child Health J, 12,* 342-56.

Mendelson, S. (2008). A Community-Based Parish Nurse Intervention Program for Mexican American Women with Gestational Diabetes.

Metzger, B. (2007). Summary and Recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care, 30(2),* S251-S260.

Moyer, V. (2014). Screening for Gestational Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine, 160(6),* 414-20.

Naylor, C.D. (1996). Cesarean Delivery in Relation to Birth Weight and Gestational Glucose Tolerance. *JAMA, 275(15),* 1165-70.

Ockene, I. (2012). Outcomes of a Latino Community-Based Intervention for the Prevention of Diabetes: The Lawrence Latino Diabetes Prevention Project. *American Journal of Public Health, 102(2),* 336-42.

Office on Women's Health (2013). "Prenatal Care Utilization 2013." Health Resources and Services Administration. Retrieved from http://mchb.hrsa.gov/chusa13/health-services-utilization/p/prenatal-care-utilization.html

Oostdam, N. (2011). Interventions for Preventing Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Journal of Women's Health, 20(10),* 1551-63.

Ostlund, I. (2004). Gestational diabetes and preeclampsia. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 13(1),* 12–16.

Passel, J. and Taylor, P. (2009). "Who's Hispanic?" Pew Research Center. Retrieved from http://www.pewhispanic.org/2009/05/28/whos-hispanic/

Perichart-Perera, O. (2009). A Medical Nutrition Therapy Program Improves Perinatal Outcomes in Mexican Pregnant Women With Gestational Diabetes and Type 2 Diabetes Mellitus. *The Diabetes Educator, 35(6):* 1004-13.

Perichart-Perera, O. (2012). Low Glycemic Index Carbohydrates versus All Types of Carbohydrates for Treating Diabetes in Pregnancy: A Randomized Clinical Trial to Evaluate the Effect of Glycemic Control. *International Journal of Endocrinology, 2012*: 1 - 12. doi: doi:10.1155/2012/296017

Petersen, A. (2005). Correlates of Physical Activity among Pregnant Women in the United States. *Medicine & Science in Sports & Exercise*, 1748-53. doi: 10.1249/01.mss.0000181302.97948

Pettitt, D.J. (1983). Excessive obesity in offspring of Pima Indian women with diabetes during pregnancy. *N Engl J Med, 308(5),* 242-5.

Prince, S.A. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity* 2008, **5**:56

Reyes, E. (2012). Early Intensive Obstetric and Medical Nutrition Care Is Associated with Decreased Prepregnancy Obesity Impact on Perinatal Outcomes. *Gynecol Obstet Invest, 73:* 75-81.

Rhoads-Baeza, M.E. and Reis, J. (2010). An exploratory mixed method assessment of low income, pregnant Hispanic women's understanding of gestational diabetes and dietary change. *Health Education Journal, 71(1),* 80-9.

Ros, H.S. (1998). Comparison of Risk Factors for Preeclampsia and Gestational Hypertension in a Population-based Cohort Study. *American Journal of Epidemiology, 147(11)*: 1062-72.

Ruchat, S. and Mottola, M. (2013). The important role of physical activity in the prevention and management of gestational diabetes mellitus. *Diabetes Metab Res Rev, 29,* 334-46.

Ruggiero, L. (2011). Community-Based Translation of the Diabetes Prevention Program's Lifestyle Intervention in an Underserved Latino Population. *The Diabetes Educator, 37(4),* 564-72.

Siega Riz, A.M. (2009). A systematic review of outcomes of maternal weight gain according to the Institute of Medicine recommendations: birthweight, fetal growth, and postpartum weight retention. *Am J Obstet Gynecol, 201*, 339.e1–14.

Thornton, P. (2006). Weight, Diet, and Physical Activity-Related Beliefs and Practices Among Pregnant and Postpartum Latino Women: The Role of Social Support. *Maternal and Child Health Journal, 10(1),* 95-104.

Tieu, J. (2011). Dietary advice in pregnancy for preventing gestational diabetes mellitus. *Cochrane Database of Systematic Reviews, 2,* 1-32. doi: 10.1002/14651858.CD006674.pub2

Tobias, D. (2011). Physical Activity Before and During Pregnancy and Risk of Gestational Diabetes Mellitus. *Diabetes Care, 34(1),* 223-9.

Tovar, A. (2009). The Impact of Gestational Weight Gain and Diet on Abnormal Glucose Tolerance During Pregnancy in Hispanic Women. *Matern Child Health J, 13(4):* 520-30.

Turok, D. (2003). Management of Gestational Diabetes Mellitus. *Am Fam Physician, 68(9)*: 1767-73.

United Nations (2008). "Official list of MDG indicators." Retrieved from http://mdgs.un.org/unsd/mdg/Host.aspx?Content=Indicators/OfficialList.htm

Vercoza Viana, L. (2014). Dietary Intervention in Patients With Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis of Randomized Clinical Trials on Maternal and Newborn Outcomes. *Diabetes Care, 37:* 3345 - 55.

Vincent, D. (2014). The Effects of a Community-Based, Culturally Tailored Diabetes Prevention Intervention for High-Risk Adults of Mexican Descent. T*he Diabetes Educator, 40(2),* 202-13.

Wagner, L. (2004). Diagnosis and Management of Preeclampsia. *Am Fam Physician, 70(12),* 2317-24. http://www.aafp.org/afp/2004/1215/p2317.html

Wendland, E.M. (2011). Interventions for the prevention of type 2 diabetes mellitus in women with previous gestational diabetes. *Cochrane Database of Systematic Reviews* 2011, 8, 1-8. doi:10.1002/14651858.CD009283

WHO (2015). “Diabetes: the cost of diabetes.” Fact Sheet No. 236. Retrieved from http://www.who.int/mediacentre/factsheets/fs236/en/

WHO (2015). “Noncommunicable diseases.” WHO Fact Sheet. Retrieved from http://www.who.int/mediacentre/factsheets/fs355/en/

World Bank (2015). “Latin America & Caribbean: Data.” Retrieved from http://data.worldbank.org/region/LAC

Yogev, Y. (2004). The association between preeclampsia and the severity of gestational diabetes: The impact of glycemic control. *AJOG, 191(5),* 1655–1660.

Zhang, C. (2006). Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. *Diabetes Care, 29(10):* 2223 - 30.

Appendix A: Table of the characteristics of included studies.

Prevention of GDM				**Management of GDM**		
	Chasan-Taber et al., 2008	**Chasan-Taber et al., 2014**	**Reyes et al., 2012**	**Bung et al., 1991**	**Mendelson et al., 2008**	**Perichart-Perera et al., 2009**
Study Design	Prospective cohort	Prospective cohort, Proyecto Buena Salud	Retrospective cohort	Randomized controlled trial	Randomized controlled trial	Quasi-experimental study, historical control
Total subjects (N)	1006	1241	546	34	100	174
Cases of GDM (n)	33	57	58	34 (inclusion criteria)	100 (inclusion criteria)	39 (47 with type 2 diabetes)
Cases of AGT (n_1)	119	175				
GDM diagnostic criteria	ADA 2004; 1-hr OGTT >180 mg/dL; fasting blood glucose >105 mg/dL or 2-hr postprandial blood glucose >120 mg/dL	ADA 2004	ADA 2004	3-hr glucose tolerance test (no additional details provided)	Not reported	ADA 2004 or 1-hr glucose screening test result ≥ 180 mg/dL
Predominant Country of Origin	Puerto Rico	Restricted to women of Puerto Rican or Dominican Republic heritage	Mexico	Not reported	Mexico	Mexico
Study Population	Hispanic prenatal care patients, age 16-40, <24 weeks gestation in Massachusetts	Hispanic prenatal care patients, age 16-40, <20 weeks gestation in Massachusetts	Urban Mexican prenatal care patients, ≤13 weeks gestation in Mexico	Hispanic prenatal care patients in California with GDM and persistent elevated fasting blood glucose despite an ADA diet	Mexican American prenatal care patients with GDM, age 18-40, between 12-32 weeks gestation	Mexican prenatal care patients with GDM or type 2 diabetes, ≤ 29 weeks gestation

Exposure	Physical activity; Household/caregiving, occupational, sports/exercise, active living, and total physical activity	Physical activity; Met ACOG exercise guidelines, total physical activity, moderate-intensity activity, vigorous intensity activity, household/caregiving, occupational, and sports/exercise	Women with overweight (OW) and obese (OB) pre-pregnancy BMI who underwent a medical nutrition program with intensive obstetric care	Exercise and diet	Parish nurse intervention program – social/spiritual support and enhanced education about GDM management using medical nutrition diet recommendations	Medical nutrition therapy (MNT) – individualized nutritional counseling and glucose self-monitoring
Control	Referent group was women in the category of least physical activity	Referent group was women in the category of least physical activity	Women with normal weight (NW) pre-pregnancy BMI who received standard prenatal care	Insulin therapy and diet	Care as usual - clinic's standard education for women with GDM	Historical controls from medical charts
Timing of exposure	Assessed for pre-pregnancy (1 year prior to pregnancy), early pregnancy (mean=15 weeks gestation), and mid-pregnancy (mean=28 weeks gestation)	Assessed for pre-pregnancy (1 year prior to pregnancy), early pregnancy, and mid-pregnancy (mean=21.3 weeks gestation)	Initiated within 2 weeks of admission to prenatal care and continued throughout pregnancy	Initiated at enrollment (mean gestational age=30.3 weeks at enrollment); total duration not reported	Not reported	From admission to study until end of pregnancy
Exposure assessment method/tool(s)	Modified Kaiser Physical Activity Survey (validated for use in pregnancy); 5-level categorical	Modified Pregnancy Physical Activity Questionnaire (validated for use in pregnancy);	Measurement of adherence to nutrition recommendations not reported	Direct observation of exercise in a lab	Attendance at education sessions; Measurement of adherence to nutrition recommend	Pass 24-hour recall assessed diet every month; Also a questionnaire about

	scale; higher score = more frequent activity	Semi-quantitative – total physical activity measured in MET-hrs/day			ations not reported	diet adherence
Primary outcome(s)	GDM	GDM and AGT	Miscarriage, hypertensive disorders, premature rupture of membranes, preterm birth, stillbirth, GDM, large- or small-for-gestational-age	Gestational age at delivery, mode of delivery, birth weight and length, macrosomia, and neonatal hypoglycemia	The Health Promoting Lifestyle Profile II (includes categories such as health responsibility and physical activity), glycemic control, macrosomia, days of hospitalization	Insulin requirement, glycemic control, gestational age at delivery, birth weight, macrosomia, preeclampsia, hospitalization, perinatal morality
Secondary outcome	AGT					
Model covariables	Age and pre-pregnancy BMI	Age, pre-pregnancy BMI, and total gestational weight gain				Gestational age, history of miscarriages, parity, insulin use at baseline
Main results	No significant association between total physical activity and risk of GDM, however, women in highest quartile of household/caregiving during pre-pregnancy and mid-	No significant association between total physical activity or meeting physical activity guidelines and risk of GDM; Women in the highest	OB women had the greatest odds of developing GDM when compared to NW women (OR 4.2, 95% CI 1.9-9.3), they were also most likely to have preeclampsia (OR 3.3, 95%	No significant difference in weekly blood glucose measurements between groups; none of the 17 participants	The intervention group had a significant increase in HPLP II score from pre to post-intervention (p=0.016); there was no significant pre-post	Lower odds of having low birth weight infants among GDM women in MNT group compared to control; lower

	pregnancy had lower risk (adjusted) of GDM compared to women in lowest quartile (OR 0.2, 95% CI 0.1-0.8); Also, women in highest quartile for sports/exercise during mid-pregnancy had lower risk of GDM compared to women in lowest quartile (OR 0.1, 95% CI 0.0-0.7)	quartile of moderate-intensity activity during early pregnancy had lower risk (adjusted) of AGT compared to women in lowest quartile (OR 0.48, 95% CI 0.27-0.88); Women in highest levels of occupational activity in early pregnancy had lower risk (adjusted) of AGT compared to unemployed women (OR 0.48, 95% CI 0.28-0.85)	CI 1.2-8.8), and have lack of spontaneous labor (OR 2.4, 95% CI 1.5-3.8); NW women had the lowest incidence of planned cesarean sections	compliant in the intervention group required insulin; rates of perinatal complications were similar between groups	intervention change in fasting blood glucose or hemoglobin A1c; there was no significant difference between groups in the number of hospitalization days or incidence of macrosomia	odds of preeclampsia and NICU admissions among women in MNT group compared to control

Appendix B: Table of the characteristics of additional articles based on the Latina Gestational Diabetes Mellitus Cohort data, included in the qualitative summary.

	Gollenberg et al. 2010	**Tovar et al. 2009**
Total subjects (N)	1006	813
Exposure	Sedentary behaviors during pre-, early, and mid-pregnancy	Gestational weight gain, diet
Control	Referent group was women in the least sedentary group for each category	Referent groups: women who met recommended weight or dietary goals and those with normal glucose tolerance
Exposure assessment method/tool(s)	Modified KPAS; sedentary behavior included hours of TV watching, sitting at work, and reverse-scored participation in sports/exercise; total sedentary score calculated as a composite of all three categories	Semi-quantitative food frequency questionnaire that captured the first half of pregnancy (validated for use with Hispanics in Northeastern US); weight measured during prenatal care visits
Outcome(s) of interest	AGT	AGT
Model covariables	Maternal age, smoking, pre-pregnancy BMI, maternal education, parity	Maternal age, smoking, history of GDM, family history of diabetes, pre-pregnancy BMI, parity, gestational weight gain (for diet analyses), physical activity, and total calories (for diet analyses)
Main results	Higher total sedentary behavior compared to lower total sedentary behavior in mid-pregnancy was associated with an increased risk of AGT (OR 11.8, 95% CI 2.25-61.86); lower sports/exercise activity compared to higher sports/exercise activity in mid-pregnancy was associated with an increased risk of AGT (OR 2.01, 95% CI 1.01-4.02); no significant associations found between sedentary behavior during pre- or early pregnancy and risk of AGT	Higher pre-pregnancy BMI was associated with increased risk of AGT compared to lower pre-pregnancy BMI (OR 3.4, 95% CI 1.7-6.8 and p_{trend} <0.001); no significant relationship between overall meeting target weight or rate of weight gain and risk of AGT, however, class II/III obese women with high weight gain or who exceeded target weight were more likely to develop AGT compared to woman who gained within IOM guidelines (OR 4.2, 95% CI 1.1-16, OR 3.2, 95% CI 1-10.5, respectively); after controlling for weight gain, higher intake of saturated fat and fiber, and lower intake of energy-dense snack foods and polyunsaturated fat:saturated fat ratio were associated with a significantly increased risk of AGT