2017

Non-Pharmacologic Measures to Prevent and Treat Gestational Diabetes

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NON-PHARMACOLOGIC MEASURES TO PREVENT AND TREAT GESTATIONAL DIABETES

A MASTER'S PROJECT

SUBMITTED TO THE GRADUATE FACULTY

OF THE GRADUATE SCHOOL

BETHEL UNIVERSITY

BY

DIKSHYA ARYAL

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF SCIENCE IN NURSE-MIDWIFERY

MAY 2017

BETHEL UNIVERSITY

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May 2017

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Acknowledgements

It is my great pleasure to acknowledge the help, support, encouragement, and mentorship of the various individuals with whom I enjoyed this journey of graduate study in nurse-midwifery. First, I would like to thank my family for always being there for me. My husband has been a constant source of encouragement and deserves special mention. He not only supported and encouraged me throughout this journey, but also worked with me to overcome the many roadblocks that I encountered. With every difficulty I faced, he would suggest things to try to overcome them. Without his support, I would not have been able to complete this journey.

Secondly, I would also like to thank my parents and sisters for their love and care. Since childhood, my mom has always encouraged me to dream big and to achieve greater success in life. To my dad, who always supported me in my decision and helped nurture me to be the individual that I am today. To my sister Aarya, who introduced me to the profession of nursing and for being my role model. To my sister Richa, who has been a special friend and has always been with me through my ups and downs.

Next, I would like to thank my Bethel family for their support and encouragement. I would like to thank my faculty, who encouraged me throughout this journey and who helped me succeed. To Katrina Wu, Dr. Julie Ann Vingers, Laurel McKeever, Lisa VanGerpen, and Chad, Peterson, who trained and guided my development throughout my midwifery education. My advisor, Dr. Jane Wrede, deserves a special mention for her encouragement and mentorship. I am also thankful to my classmates. We helped each other and shared both our failures and success stories, and kept ourselves motivated. I am grateful that I was a part of this special cohort and firmly believe that we will all succeed in becoming great midwives and in serving our community with distinction.

I am also fortunate to have been mentored by so many brilliant providers during this journey. I would like to thank them all for their selfless teaching of midwifery practical skills, OB/GYN, and women's health. To Carrie Kneisl of Southside Community Health Services, who was patient with me and who first introduced to midwifery. Carrie guided me through my first step into the world of midwifery. To Dr. Teresa Albert of Monticello Clinic, who taught me OB/GYN skills and who allowed me flourish in her practice. To Charlotte Rollie of Essentia Health-Park Rapids, who guided me through the childbirth process and who helped me learn so many midwifery skills that will remain with me throughout my life. To Cheryl Heitkamp of Willow Birth Center, who helped me further my knowledge and skills in midwifery. To Dr. Dennis Hartung of Western Wisconsin Health, who took me under his wing and let me further develop my clinical skills. The experience that I acquired at his practice, including the breech delivery, will forever guide me as I start my own midwifery practice.

Finally, I would like to thank God for helping me overcome all my struggles and for enabling me to embark upon this journey of midwifery practice. I am extremely grateful and humble. I believe that I am truly blessed to have received all the help, support, encouragement, and mentorship that I have received from so many wonderful people.

Abstract

Background: Gestational Diabetes (GDM) can have adverse effects on the health of both mother and baby during pregnancy and for a lifetime thereafter. While insulin is the mainstay of treatment, metformin and glyburide may be considered as alternatives (Carroll & Kelley, 2014). Pregnant mothers, however, may be hesitant to use pharmaceutical therapies, preferring natural alternatives (Zaki & Albarraq, 2014).

Purpose: The purpose of this paper is to identify and examine effective non-pharmacological interventions for the prevention and the management of GDM.

Results: Twenty-one articles were included in this review and thirteen studies support the use of certain diets (Mediterranean or Dash diets), and dietary supplements (myo-inositol, probiotics, and vitamin D supplementation) in the prevention and management of GDM. The other eight articles support the use of lifestyle modifications (sleep, physical exercise, yoga), and lifestyle intervention (counseling) in the prevention of GDM.

Conclusions: The review found that diets (Mediterranean and Dash diets), dietary supplements (myo-inositol, probiotics, and vitamin D), lifestyle modifications (physical exercise, yoga, sleep), and lifestyle interventions show promising results in the prevention and management of GDM.

Implications for Practice: Nurse-midwives should remain up-to-date on major interventions and current research trends of GDM, thus safeguarding the health and safety of both pregnant mother and her baby. The findings of this review have implications for nurse-midwives who are working with mothers that are hesitant to use pharmaceutical therapies and prefer alternatives.

Keywords: GDM, non-pharmacological, lifestyle intervention, Mediterranean diet, exercise, myo-inositol, vitamin D, probiotics, sleep

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Chapter I: Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance occurring during pregnancy (Coustan, 2017). Due to the insulin demands of the fetus, which is highest during the third trimester, women who are already insulin resistant are unable to increase their rate of insulin secretion, thus resulting in higher maternal blood glucose levels. As a result, GDM develops in women whose pancreatic functioning is insufficient to overcome the insulin resistance associated with pregnancy (Coustan, 2017). In most cases, this insulin resistance resolves within hours of delivering the baby, suggesting that GDM is due to the effects of placental hormones (Fraser & Heller, 2007). However, for many women of reproductive age, GDM can persist, potentially resulting in chronic complications. In addition, evidence shows that women with recurrent GDM over multiple pregnancies have a 60% chance of developing Type II diabetes mellitus later in life (Coustan, 2017).

Globally, GDM affects 15% of pregnancies, while in the United States, it affects 2–10% of pregnancies (Carroll & Kelley, 2014). Therefore, midwives today need to be well-informed about the effectiveness of various GDM management practices to safeguard the health of both the pregnant mother and the baby. Early detection of GDM is necessary as it can have adverse effects on the health of both mother and baby, both during pregnancy and chronically thereafter. Women with glucose intolerance during pregnancy are at increased risk of long-term adverse health outcomes, including the development of Type II diabetes mellitus, cardiovascular diseases, and metabolic syndrome (Lindsay et al., 2015). The high maternal blood glucose is associated with macrosomia, a condition in which the neonate's birth weight is a significantly heavier than usual (i.e., >4,000 g). In addition, fetal hypoglycemia (i.e., fetal plasma glucose <30 mg/dl), stillbirths, and other morbidities during the neonatal period can also contribute to a

high maternal blood glucose level (Carroll & Kelley, 2014). Children born to mothers with GDM have also been shown to have an increased risk for the development of diabetes and metabolic syndrome later in life (Bone, 2015).

During pregnancy, mothers may be hesitant to use pharmaceutical therapies and may prefer other alternatives (Zaki & Albarraq, 2014). In a study of 760 pregnant women attending an obstetric clinic, the majority of pregnant women (78.9%) believed that limiting the use of medications during pregnancy was preferable for overall fetal health (Zaki & Albarraq, 2014). Therefore, the purpose of this paper is to review research papers in order to determine whether non-pharmacological treatments are effective in the prevention and treatment of GDM.

One of the most common non-pharmacological treatments for preventing and treating GDM is diet. Special diets for GDM include the Dash and Mediterranean (MED) diets. The Dash diet is a low glycemic index and low energy dense diet containing high quantities of phytoestrogens, magnesium, potassium, and dietary fiber (Izadi et al., 2016). Similarly, the MED diet includes the consumption of fruits, vegetables, legumes, whole grains, and foods rich in monounsaturated fatty acids. It is also associated with lower risk for several chronic diseases, including GDM (Izadi et al., 2016).

A second non-pharmacological treatment for prevention and treatment of GDM is dietary supplementation with myo-inositol, vitamin D, or probiotics. Myo-inositol is a natural form of inositol found in fruits and has been found to be helpful in glycemic control (Brown, 2016). Vitamin D helps in the metabolism of calcium and phosphorus, and is associated with the metabolism of glucose (Zhang et al., 2016). Probiotics are live microbial supplements that improve the intestinal microbial balance. They have also been found to have positive effect on metabolism, and the prevention of type II diabetes and GDM (Dolatkhah et al., 2015).

A third non-pharmacological treatment for preventing GDM includes lifestyle interventions, such as exercise, sleep, and counseling. Physical exercise and yoga helps to promote blood circulation and improves insulin sensitivity, resulting in the increased utilization of glucose by muscle cells (Sununta, Sasitorn, & Thitiporn, 2014). A yoga exercise program, using *pranayama* (deep-breathing) and *asanas* (posture and movement) techniques, has been developed for pregnant women with GDM (Sununta et al., 2014). Counseling is arguably one of the more significant approaches to the management of diabetes, resulting in the empowerment of women with the knowledge and tools needed to optimize their own health while reducing adverse pregnancy outcomes (Mills, Palmer, & Arya, 2015). A discussion of the role of diet, body mass index (BMI), and exercise with these patients would be helpful in facilitating the management and treatment of patients with GDM (Mills et al., 2015).

Statement of Purpose

The purpose of this paper is to examine and identify literature pertaining to the effective non-pharmacological management (i.e., prevention and treatment) of GDM. Specifically, this review focuses on the use of diets (including the Dash and MED diets), dietary supplementation (using myo-inositol, vitamin D, and probiotics), exercise (i.e., cardio, yoga), and sleep in the management of GDM.

Evidence Demonstrating Needs

The American College of Obstetrician and Gynecologists (ACOG), International Diabetes Federation (IDF), Canadian Diabetes Association (CDA), and the British National Institute of Health and Care Excellence (NICE) recommend diet therapy as the first line treatment for GDM to achieve normal blood glucose levels (Carroll & Kelley, 2014). Diet has been shown to have a positive impact on both the prevention and treatment of mild GDM.

Nutrition therapy is a key component of the management of GDM and influences pregnancy outcomes in mother and child (Shi et al., 2016). Dietary supplementations (e.g., myo-inositol, vitamin D, and probiotics) during pregnancy have also been studied as potential treatments and preventative measures for GDM. However, a Cochrane review found insufficient evidence to support the use of myo-inositol, vitamin D, and probiotics as treatments for GDM (Coustan, 2016).

Furthermore, the ACOG, IDF, CDA, and NICE recommend that insulin should be considered for the management of GDM if dietary interventions prove inadequate (Carroll & Kelley, 2014). However, many women are disinclined to use insulin due to fear of needles and injections, an unwillingness to receive several injections a day, the burdensome cost of insulin therapy, and fears of insulin-related hypoglycemia (Carroll & Kelley, 2014). The IDF and CDA list metformin and glyburide as alternatives for insulin non-adherent women (i.e., those who refuse to take insulin) and in cases where insulin might be considered unsafe (Carroll & Kelley, 2014). However, the long-term effects of these drugs on the mother and baby have not yet been studied (Carroll & Kelley, 2014).

Informed consent is a legal and ethical requirement. It is the health care provider's responsibility to provide adequate information to the patient so that the patient is able to process the information and make an appropriate decision (Ryan, 2017). Informed consent helps to protect the patient's right of self-determination (Ryan, 2017). Therefore, women should be presented with all the evidence for various GDM treatment methods and have the right to choose what method they believed to be best for their health and that of their baby.

Significance to Nurse-Midwifery

The position statement of the American College of Nurse-Midwives (ACNM) states that nurse-midwives are primary care providers who "are accountable for addressing the majority of health care needs, developing sustained partnerships with patients, and practicing within the context of family and community" (ACNM, 2012, p. 21). Moreover, "health promotion, disease prevention, and health education" (ACNM, 2013, p. 2) is one of the hallmarks of nurse-midwifery. Therefore, as a health care provider, the nurse-midwife should be aware of the risk factors, criteria for diagnosis, prevention, and treatment of GDM.

Midwifery practice should include the routine screening and diagnosing of GDM. The US Preventative Services Task Force (USPSTF, 2016) recommends screening pregnant women after 24 weeks gestation for GDM. Before 24 weeks gestation, there is insufficient evidence of the benefits and harms of screening (USPSTF, 2016).

ACOG recommends a two-step process for GDM screening and diagnosis. This two-step process involves a one-hour glucose challenge test and a three-hour glucose tolerance test (GTT) (Coustan, 2017). In the one-hour glucose challenge test, pregnant women are provided with a 50 g oral glucose load without regard to the time of day. If the blood glucose level is >140 mg/dl one-hour post-ingestion, the three-hour GTT should be performed (Coustan, 2017). This GTT involves the oral administration of a 100 g oral glucose load, following which plasma serum glucose is measured at fasting, and at one, two and three hours post-administration. In three hour GTT, glucose threshold concentration at fasting is 95 mg/dl, at one hour is 180 mg/dl, at two hours is 155 mg/dl, and at three hours is 140 mg/dl. When at least two of these glucose thresholds have been met and exceeded, the diagnosis of GDM is confirmed (Kim & Floyd, 2015).

Furthermore, midwifery practice remains up-to-date on the latest standards of care in the prevention and treatment of GDM, incorporating new "scientific evidence into clinical practice" (ACNM, 2013, p. 2). This use of evidence-based practice is also one of the hallmarks of nurse-midwifery. This comprehensive literature review analyzes natural therapies, such as diet (e.g., Dash and MED), dietary supplements (e.g., myo-inositol, vitamin D, probiotic), exercise (e.g., physical activity, yoga), and sleep for the prevention and treatment of GDM. This research is also congruent with another hallmark of nurse-midwifery: "incorporation of evidence-based complementary and alternative therapies in education and practice" (ACNM, 2013, p. 2).

Theoretical Framework

King's theory of goal attainment (TGA) provides an appropriate theoretical framework for the prevention and treatment of GDM. TGA focuses on the process used to guide the nurse-patient relationship toward the attainment of certain life goals. This theory promotes patient-family-centered care that encourages collaboration among health care professionals, patients, and their families (Caceres, 2015; King, 1981). Furthermore, patient-family-centered care promotes patient satisfaction by encouraging the patient and their family to engage in open communication with health care providers (Leon-Demare, MacDonald, Gregory, Katz, & Halas, 2015).

King's TGA relies on four basic assumptions. The first assumption is that goals are attained through nurse-patient interactions. The second assumption is that both the nurse and the patient must recognize each other, and that there must be congruence between their role expectations and role performance. The third assumption is that the nurse uses their knowledge and skills to set goals in collaboration with the patient and that they communicate information to the patient. The last assumption is that the nurse is proactive in helping the patient to achieve their preset goals (Caceres, 2015).

King's theory is congruent with the assessment, diagnosis, planning, implementation, and evaluation stages of the nursing process. The assessment phase is represented by concepts of perception, judgment, action, and reaction. In this phase, the nurse and the patient begin the process of interacting with one another and form initial judgments about one another. These actions and reactions are made on the basis of the perceptions and judgments, which are a product of the thoughts that the nurse and patient have about one another's motives, behaviors, and goals. The diagnosis phase consists of the nurse querying the patient's environment, personal, and interpersonal systems (Caceres, 2015). During implementation phase, the nurse and the patient follow their mutually agreed plan. In the evaluation phase, the nurse and patient look to determine whether their goals have been achieved. If these goals are found not have been achieve, the nurse and patient review that factors that might have affected the achievement of these goals (Caceres, 2015).

King's theory is based on the notion that the patient must always be involved in their own care, and that all clinical decision making at every stage of care is patient-centric. Therefore, King's theory suggests that nurses work hand-in-hand with their patients to set and meet mutual goals for the benefit of the patient's good health (Leon-Demare et al., 2015).

Summary

GDM is a serious condition which, if not well maintained by controlling blood glucose levels, can result in various complications to both the mother and her baby. Therefore, it is very important to prevent, manage, and treat GDM. As primary health care providers, midwives should be aware of the risk factors, diagnosis, prevention, and treatment of GDM, including the non-pharmacological and natural therapy approaches that are increasingly being sought after by

patients. The adoption of these natural and non-pharmacological treatments, if efficacious, may be helpful in reversing the alarming spike in the incidence of GDM over recent years.

The following chapter will outline the methods used to explore the literature, describing the process by which original research studies that provide evidence of non-pharmaceutical intervention for GDM were identified. These research studies, their relative strengths and limitations, as well as subsequent recommendations for practice are addressed in Chapter 3. Chapter 4 provides a synthesis of the studies that answer the research question, identifies gaps in the research literature, explores the implications of this knowledge for midwifery practice, and offers a number of recommendations for future areas of study.

Chapter II: Methods

The purpose of this chapter is to describe the methods used to identify research studies for review and to inform the investigation of what non-pharmacological measures might be effective for preventing and treating GDM. A total of 35 original research articles were identified from a search of multiple databases as satisfying the search term parameters. Of these 35 research studies, 21 met the inclusion criteria for this literature review.

Search Strategies

The literature review incorporated studies published between 2011 and 2016. The databases used for the search were CINAHL, CINAHL PLUS, ScienceDirect, Ovid, Google Scholar, the Cochrane Database of Systematic Reviews, and PUBMED MEDLINE. Keywords were searched in combination using Boolean operators. These keywords, and the number of articles for these keywords, include: gestational diabetes mellitus (21 articles), gestational diabetes mellitus and prevention (21 articles), vitamin D and gestational diabetes mellitus (four articles), gestational diabetes and probiotics (two articles), diet and exercise and gestational diabetes (three articles), yoga and gestational diabetes mellitus (one articles), lifestyle intervention and gestational diabetes mellitus (three articles), sleep and gestational diabetes mellitus (two articles), MED diet and diabetic diet (three articles), and myo-inositol and diabetes (three articles).

Criteria for Inclusion and Exclusion

The articles selected for this literature review were included based on their description of effective non-pharmacological measures for the prevention and treatment of GDM. Factors such as the quality of the original research, strength of findings, scientific rigorousness, and the age of the study were used as inclusion criteria. Following this criteria, only research studies published

in the last 6 years (i.e., 2011–2016) were included. One research article from 2008 is included due its strength of its findings.

Many of the research articles identified in the initial search as having been related to the research topic had to be excluded because they failed to satisfy scientific rigor, presented weak or inconclusive findings, or demonstrated poor research quality. A second search of the databases was made using the same search string, but having relaxed the criteria for date of publication in the hope of finding strong original research studies. Many of the articles found, however, were simply duplicates of the studies already included, while other studies failed to satisfy the inclusion criteria.

Summary of Selected Studies

The articles included in this review consisted of 14 randomized controlled trials (RCTs), one quasi-experimental trial, two prospective cohort studies, two case controlled studies, one cohort study, and one prospective observational non-interventional study. The selected studies were performed in various countries across North America, Europe, and Asia. Preference was given to studies performed in the US; however, due to low number of articles related to the research question, only five of the 20 research studies included in this review were performed in the US. The remainder of the studies were, for the most part, performed in developed countries with similar living conditions and medical facilities as those found in the US, thus enabling the findings of this study to be generalized to the US. Italy and China had three studies each; Finland and Iran had two studies each; while Spain, Greece, Turkey, Thailand, and India each had one study.

Evaluation Criteria

The Johns Hopkins Research Evidence Appraisal Tool was used to evaluate the quality of the selected research articles (Dearholt & Dang, 2012). The level of evidence for the 21 selected articles was appraised on a scale ranging from I to IV on the basis of their quality. Level I studies include experimental studies, RCTs, and systematic reviews of RCTs—with or without meta-analysis. Level I studies are regarded as the highest quality research (Dearholt & Dang, 2012). This implies consistency among generalized results: that the sample size is sufficient for the study design, that there are adequate controls in place, that the conclusions are definitive, and that the subsequent recommendations are consistent.

Level II includes quasi-experimental studies and systematic reviews of multiple RCTs and quasi-experimental studies in combination, or quasi-experimental studies only, with or without meta-analysis (Dearholt & Dang, 2012). These research studies are considered to be good quality, with reasonably consistent results, a sufficient sample size for the study design, and fairly definitive conclusions that lead to reasonably consistent recommendations (Dearholt & Dang, 2012).

Level III includes non-experimental studies and systematic reviews of multiple RCTs, quasi-experimental, and non-experimental studies in combination, or non-experimental studies only, with or without meta-analysis (Dearholt & Dang, 2012). These studies are considered low quality, with poor quality evidence producing inconsistent results, the sample sizes for these studies are often insufficient for the study design, and few definitive conclusions can be drawn (Dearholt & Dang, 2012).

Level IV includes the opinions of respected authorities. This includes nationally recognized expert committees and/or consensus panels based on scientific evidence. Level IV

has three sub-categories, allowing such evidence to be graded low, good, or high quality (Dearholt & Dang, 2012).

Summary

Various databases were used in the search process to identify research articles focuses on non-pharmacological measures for the prevention and treatment of GDM. Factors such as the quality of the study, strength of findings, scientific rigorousness, and the age of the study were used to select the final 21 articles that met the inclusion criteria. The John Hopkins Research Evidence Appraisal Tool was used to evaluate the quality and the level of evidence of the selected research articles.

The Chapter Three will provide an analysis and discussion of the selected twenty-one research studies. These research studies, their relative strengths and limitations, as well as subsequent recommendations for practice are addressed in the chapter. Chapter 4 provides a synthesis of the studies that answer the research question, identifies gaps in the research literature, explores the implications of this knowledge for midwifery practice, and offers a number of recommendations for future areas of study.

Chapter III: Literature Review and Analysis

This chapter provides an analysis and discussion of the selected research studies through the matrix method. This discussion will outline the purpose of the study, the study design, and will provide a synthesis of the major findings. At the end of the chapter, the strengths and weaknesses of the studies are evaluated.

Synthesis of Matrix

Twenty-one scholarly research studies used were organized in a matrix (see Appendix I). For each study included in the matrix, the purpose of study, sample size, design, level of measurement, results, conclusions, recommendations, and the level and quality of the study (per the appraisal tool) have been clearly noted. Organizing the research studies in such a matrix facilitates the assessment and synthesis of findings.

Synthesis of Major Findings

All the studies chosen for this review are concerned with non-pharmacological preventative measures for GDM. Thirteen studies included in this review support the use of certain diets and supplements—such as the MED diet and supplementation with myo-inositol, probiotics, or vitamin D—in the prevention and management of GDM. The remaining eight articles explore and support the use of lifestyle modifications—such as modifying sleep duration, physical exercise, and yoga—in the prevention of GDM, with these interventions having been shown to impact blood glucose regulation in GDM.

The following sub-section synthesizes the major findings in relation to diet, dietary supplementation, and lifestyle modifications.

Diet and Supplementation

Thirteen studies were based on diet and the use of various dietary supplements for the prevention of GDM. These studies include MED and Dash diets, and supplementation with myo-inositol, vitamin D, or probiotics.

MED and Dash diets. These diets are representative of centuries old patterns of eating and include mostly plant-based foods. The MED diet is incorporates nutrient-dense foods, including fruits, vegetables, legumes, nuts, and whole grains. Olive oil is the main source of fat in the MED diet. Furthermore, the MED diet includes foods that are rich in omega-3 fatty acids and limits the amount of red meat and other animal products (Benson, Pereira, & Boucher, 2011).

There are a number of health benefits to the MED diet, such as a reduction in the incidence and prevention of diabetes, and global improvements in cardiovascular system health (Benson et al., 2011). This specific diet has also been shown to have a positive effect on insulin sensitivity as a results of having replaced saturated fats and trans fats with unsaturated fats (Benson et al., 2011). While diet is safe during pregnancy and should provide adequate folic acid, pregnant women are recommended to supplement their prenatal intake of vitamin B12, either through dietary supplements or by increasing their intake of animal-based foods (e.g., red meat, fish, eggs) while on the MED diet (Balci et al., 2014).

The Dash diet includes foods that are low in total fat, saturated fat, and cholesterol. It also includes plenty of fruits, vegetables, and whole grains. In the Dash diet, dietary protein is sources from low fat dairy products, fish, and nuts (Harvard, 2015). The Dash diet is high in fiber, magnesium, potassium, and calcium, while being low in sodium. The Dash diet has many

benefits and promotes overall health; moreover, the Dash diet is best suited for those with hypertension and is considered safe for use during pregnancy (Harvard, 2015).

This critical review evaluated two studies that assessed the effectiveness of the MED diet and a further two studies that assessed the effectiveness of the Dash diet for the prevention of GDM. One of the studies exploring the effectiveness of the MED diet was evaluated as level I evidence, while the study was level II.

In the level I case control hospital-based study by Izadi et al. (2016), two groups of pregnant women were studied: one group with GDM (n = 200) and the other without GDM (n = 260). The study showed that the MED diet was negatively related to fasting blood glucose levels, hemoglobin A1C, and serum triacylglycerol concentrations. Also, the total serum cholesterol level was lower in the third tertile of the MED diet group. Participants in the highest tertile of the MED diet group had an 80% lower risk for GDM as compared with those in the lowest tertile (p = 0.006) with $p < 0.05$ being considered statistically significant. Furthermore, adherence to the Dash diet was associated with 71% lower risk of GDM (Izadi et al., 2016).

The level II prospective observational study by Karamanos et al. (2014) employed a sample of 1076 pregnant women and explored the relationship between the MED diet and the incidence of GDM. The study showed that the incidence of GDM was lower in subjects with better adherence to the MED diet (8%) as compared to those with poor adherence (12%) (p = 0.03). The study concluded that adherence to the MED diet was associated with better glucose tolerance, even in women without GDM (Karamanos et al., 2014).

A level I RCT by Asemi, Samimi, Tabassi, Sabihi, and Esmaillzadeh (2013) explored the effectiveness of the Dash diet in preventing GDM in two group of pregnant women with GDM: Dash diet group (n = 16) and control group (n = 16). The study concluded that the Dash diet had

beneficial effects on fasting plasma glucose (FPG) and serum insulin levels in pregnant women with GDM. In this study, the Dash diet group had a lower FPG (-7.62 mg/dl) as compared to the control group (3.68 mg/dl) ($p = 0.02$). The Dash diet group also had lower serum insulin levels (-2.62 uIU/ml) as compared to the control group (4.32 uIU/ml) ($p = 0.03$) (Asemi et al., 2013).

Myo-inositol supplementation. Myo-inositol is a natural form of inositol found in fruits, vegetables, nuts, and cereal (Brown, 2016). Myo-inositol is a simple carbohydrate nutrient that the body requires for numerous cellular functions. It is available as a dietary supplement as a water soluble powder form or in capsule form and is safe to use during pregnancy (Brown, 2016).

Three research articles exploring the effectiveness of myo-inositol supplementation as a non-pharmacological prophylaxis against GDM were evaluated. All three articles were evaluated to constitute level I evidence and showed the positive effect of myo-inositol supplementation on GDM. D'Anna et al. (2015) explored the effectiveness of myo-inositol in preventing GDM in two groups of pregnant women with GDM: myo-inositol group ($n = 110$) and placebo group ($n = 110$). The main outcome measures for the study were the occurrence of GDM and insulin resistance. This study used the homeostasis model assessment (HOMA) for insulin resistance, a method for assessing insulin resistance from fasting glucose and insulin. The study showed the rate of GDM was significantly reduced in the myo-inositol group (14%) as compared with the control group (33.6%) ($p = 0.001$). Furthermore, the study found that the women who were treated with myo-inositol showed a significantly greater reduction in HOMA ($M = -1.0$, $SD = 3.1$) as compared with the women in the control group ($M = 0.1$, $SD = 31.8$) ($p = 0.048$) (D'Anna et al., 2015).

Corrado et al. (2011) found that fasting glucose levels, insulin, and HOMA were reduced in both myo-inositol ($n = 24$) and control ($n = 45$) groups. The experimental group, however, demonstrated a more significant reduction across all three dependent variables (50%) as compared the control group (29%) ($p < 0.001$). Therefore, the study supports the role of myo-inositol in improving the insulin resistance of patients with GDM (Corrado et al., 2011).

The third study is a two year prospective, randomized, open label, and placebo-controlled study involving a myo-inositol group ($n = 110$) and placebo group ($n = 110$). This study showed a significant reduction in the incidence of GDM in the myo-inositol group (6%) as compared to the placebo control group (15.3%) ($p = 0.04$) (D'Anna et al., 2013).

Vitamin D supplementation. Studies show that vitamin D influences the metabolism of calcium and phosphorus, nutrients associated with diabetes mellitus (Zhang et al., 2016). This review evaluated three studies exploring the effectiveness of vitamin D supplementation in the prevention of GDM. Vitamin D is a fat soluble vitamin that plays an important role in bone metabolism and seems to have some anti-inflammatory and immune-modulating properties (Kulie, Groff, Redmer, Hounsbell, & Schrager, 2009). Furthermore, vitamin D deficiency can cause reduced intestinal absorption of calcium and phosphorus causing bone demineralization. In adults, severe vitamin D deficiency can result in osteomalacia, and rickets in children (Dawson-Hughes, 2017). The Institute of Medicine (IOM) have set the recommended daily allowance of vitamin D at 600 international units (IU) for all women of reproductive age, including during pregnancy and lactation (Dawson-Hughes, 2017). Furthermore, adults who do not have regular year round sun exposure should consume at least 600–800 IU of vitamin D daily (Dawson-Hughes, 2017).

All three studies reviewed here are level I studies and demonstrate positive effects for vitamin D on GDM. Burris et al. (2012) associate second trimester maternal plasma levels of 25-hydroxy vitamin D (i.e., calcifediol) with GDM. In this study of 1314 pregnant women, 25-hydroxy vitamin D levels were measured during GDM screening at 26 to 28 weeks gestation. The study showed that second trimester vitamin D levels were inversely associated with glucose levels (p <0.01). Therefore, low vitamin D (i.e., 25-hydroxy vitamin D) levels may be associated with an increased risk for GDM (Burris et al., 2012).

A level I RCT by Zhang et al. (2016) also explored the effects of various doses of vitamin D supplementation on pregnant women with GDM. In the study, 133 pregnant women with GDM at 24–28 weeks gestation were randomized in four groups with different interventions. The control group (n = 20) received a placebo, while the other three groups received different amounts of vitamin D: low dose (200 IU, n = 38), medium dose (2000 IU daily for 25 days to 50000 IU in total, n = 38), and high dose (4000 IU daily and 50,000 IU every 2 weeks, n = 37). The study found that insulin, HOMA, and total cholesterol were significantly reduced in the high dose vitamin D supplementation group (p = 0.01). The results of this study support high dose vitamin D supplementation for improving insulin resistance in patients with GDM (Zhang et al., 2016).

Arnold et al. (2015) explored early pregnancy maternal vitamin D concentrations and the risk of GDM in a case-cohort study, with one group with GDM (n = 135) and another without GDM (n = 517). The investigators measured vitamin D levels at around 16 weeks of pregnancy using liquid chromatography-tandem mass spectroscopy. The study found that early pregnancy vitamin D status was inversely associated with the risk of GDM. The results showed that women with GDM had lower levels of vitamin D (M = 27.3, SD = 8.7 ng/mL) as compared to those

without GDM (M = 29.3, SD = 8.3 ng/mL) (p = 0.01). This study demonstrated a 14% reduction in the incidence of GDM with a 5 ng/mL increase of vitamin D supplementation in GDM patients. Furthermore, women with total vitamin D deficiency had a 1.97 fold increased risk for GDM (95% CI 1.12, 3.47) (Arnold et al., 2011).

Probiotic supplementation. Probiotics are live microorganisms that play an important role in health and disease, and are studied for their role in improving immune system functions and for the prevention of diarrhea (Zhang, Wu, & Fei, 2016). Studies have also shown that probiotics have glucose lowering agents that impact glucose metabolism by processing dietary polysaccharides and indigestible human enzymes (Zhang, Wu, & Fei, 2016). Furthermore, gut microbiota may also enhance glucose storage in adipose tissue by suppressing fasting induced adipocyte factor gene transcription (Laitinen, Poussa, & Isolauri, 2009). Probiotics use during pregnancy appears to be safe (Elias, Bozzo & Einarson, 2011).

This review evaluated three studies that assessed the relationship between probiotics and GDM. A level I RCT by Laitinen et al. (2009) explored the contribution of probiotics to glucose regulation during and after pregnancy, finding that probiotics may provide a prophylactic and therapeutic means of managing glucose disorder. In this study, 256 women during their first trimester were randomized into three groups to receive both a special diet and probiotics (n = 85), diet and placebo (n = 86), and placebo only (n = 85). The study found blood glucose concentrations were lowest in the diet/probiotics group (M = 4.45 mmol/l) as compared to the diet/placebo (M = 4.60 mmol/l), and placebo groups (M = 4.56 mmol/l) (p = 0.025). The finding of improved glucose tolerance in the diet and probiotic group suggests that glucose control can be improved through dietary counseling with probiotics, even among normoglycemic populations (Laitinen et al., 2009).

Another level I RCT by Dolatkhah et al. (2015) assessed the effects probiotic supplementation on glucose metabolism, finding that probiotic supplements appeared to affect glucose metabolism and weight gain in women with GDM. In this study, 64 pregnant women were randomized to receive either probiotic supplementation (n = 32) or placebo capsules (n = 32) along with dietary advice for eight consecutive weeks. The insulin resistance index in the probiotic group decreased significantly (6.74%) as compared to the placebo group, which showed an increase in insulin resistance (6.45%) ($p < 0.03$). The pattern of weight gain was similar for both groups until six weeks; in the last two weeks of the study, weight gain in the probiotic group was significantly lower (M = 0.74, SD = 0.14) as compared to the placebo group (M = 1.22, SD = 0.11) (p = 0.01) (Dolatkhah et al., 2015).

Another RCT by Lindsay et al. (2015) did not find any effect for probiotic supplementation on glycaemia control. In this study, the investigators randomized a sample of 149 women, providing the intervention group (n = 74) with probiotic capsules and placebo capsules to the control group (n = 75). Post-fasting glucose levels were the same for both intervention (M = 4.65, SD = 0.49 mMol/L) and placebo groups (M = 4.65, SD = 0.53 mMol/L) (p = 0.373) (Lindsay et al., 2015).

Lifestyle Modification

Eight studies in this review evaluated the association between GDM and lifestyle modification. The lifestyle modifications used for the prevention and treatment of GDM included sleep, yoga, exercise, and other lifestyle interventions, such as a combination of diet and exercise, and a combined counseling and education intervention for diet and exercise.

Sleep. Experimental and observational studies show evidence that both reduced and prolonged sleep are associated with impaired glucose metabolism (Rawal, Hinkle, Zhu, Albert,

& Zhang, 2016). This could be the result of elevated oxidative stress, increased systemic inflammation, energy homeostasis dysregulation, or chronic activation of the hypothalamic-pituitary-adrenal axis. Pregnant women are particularly vulnerable to sleep disturbances due to hormonal changes, physical discomfort, and the anxiety of childbirth (Rawal et al., 2016).

Two studies in this review examined the effects of sleep patterns and GDM. A prospective cohort study by Rawal et al. (2016) studied the sleep duration and napping frequency of 2581 pregnant women in the first and second trimesters. The study found that sleep duration in the first trimester was not associated with a change in the risk for GDM. However, in the second trimester, the association between sleep duration and GDM differed by pre-pregnancy obesity status ($p = 0.04$), with this association only being significant among non-obese women. Furthermore, non-obese women whose sleeping duration exceeded or was less than 8–9 hours exhibited two-fold higher risk for the development of GDM. However, the highest risk for GDM was observed among non-obese women who slept for 5–6 hours during the second trimester (Rawal et al., 2016).

A prospective cohort study by Twedt, Bradley, Deiseroth, Althouse, and Faco (2015) involving a sample of 45 women diagnosed with GDM. After assessing their sleep and blood glucose levels, the investigators found that increased sleep time was associated with lower glucose levels, while a shorter sleep duration was associated with poor glucose control in women with GDM. The study showed that an one hour increase in sleep resulted in a statistically significant reduction in fasting glucose ($p = 0.03$), post-lunch glucose ($p = 0.03$), and post-dinner glucose ($p = 0.001$) (Twedt et al., 2015).

Yoga. A yoga exercise program for pregnant women with GDM has been developed using *pranayama* (deep-breathing techniques) and *asanas* (posture and movements). These

exercises are designed for 15–20 minutes daily practice, 5 days per week for 8 weeks. *Asanas* yoga for pregnant women comprises nine postures: *padmasana*, *brahma mudra*, shoulder circling, modified *parvatasana*, modified *gomukhasana*, modified *tadasana*, modified *chakrasana*, modified *bharadvajasana*, and *dandasana.* Each posture is to be repeated ten times (Sununta, Sasitorn, & Thitiporn, 2014).

Sununta et al. (2014) assessed the effectiveness of mindful eating and yoga exercises in pregnant women with GDM, finding that mindful eating and yoga exercises were effective for promoting glycemic control. In this RCT study, a sample of 180 women with GDM were randomized to intervention ($n = 90$) and control groups ($n = 90$). The investigators found that the women with GDM in the intervention group had significantly lower fasting blood glucose levels ($M = 83.39$, $SD = 17.69$ mg/dL), postprandial blood glucose levels ($M = 105.67$, $SD = 12.93$ mg/dL), and A1C levels ($M = 5.23\%$, $SD = 0.72$ mg/dL) than those in the control group (respectively: $M = 85.85$, $SD = 17.94$ mg/dL, $p = 0.012$; $M = 112.36$, $SD = 13.15$ mg/dL, $p = 0.001$, $p < 0.05$; $M = 5.68\%$, $SD = 0.68$, $p = 0.038$) (Sununta et al., 2014).

Physical exercise. Exercise helps to increase the rate of glucose intake by the skeletal muscles and improves maternal glucose homeostasis and insulin sensitivity. Furthermore, exercise during pregnancy is associated with better glucose tolerance (Cordero, Mottola, Vargas, Blanco, & Barakat, 2015).

Cordero et al. (2015) assessed the effectiveness of maternal physical exercise (including land and aquatic activities that involve both aerobic and muscular conditioning) in preventing GDM, finding that physical inactivity was associated with an elevated risk of impaired glucose metabolism, while physical activity was associated with improved glucose metabolism. In the study, 257 pregnant women were randomized either to an intervention group ($n = 101$) with

physical exercises or to a sedentary control group (n = 156). The study found significant difference between the prevalence of GDM between the intervention (1%, n = 1) and control groups (8.8%, n = 13) (p = 0.009) (Cordero et al., 2015).

Anjana et al. (2016) also assessed the relationship between physical exercise and GDM, finding that women with GDM were significantly more sedentary (86.2%) as compared to those without GDM (61.2%) ($p < 0.001$). However, post-intervention with a sample diagnosed with GDM, there was a significant increase in physical activity ($p < 0.001$), a decrease in sedentary lifestyle ($p < 0.001$), improved glycemic control ($p < 0.001$), and a reduction in adverse neonatal outcomes (p = 0.04) (Anjana et al., 2016).

Lifestyle interventions. Lifestyle interventions focus on the prevention of GDM through counseling and education with respect to diet and exercise, and other interventions, such as weekly motivational visit and meetings (Koivusalo et al., 2016).

Koivusalo et al. (2016) conducted a level I multi-center study to assess whether a moderate lifestyle intervention could prevent the onset of GDM in pregnant women at risk of GDM. The investigators reported a reduction in the incidence of GDM by 39% in high-risk pregnant women following the intervention. In the study, 293 women meeting the following criteria were randomized either to intervention (n = 155) or control groups (n = 138): <20 weeks pregnant, history of GDM, and pre-pregnancy weight ≥30 kg/m^2. The intervention group received individualized counseling on diet, physical activity, and weight control from trained nurses, and also had one group meeting with a dietician. The control group, on the other hand, received only standard antenatal care. GDM was diagnosed in 20 intervention group participants (13.9%) and 27 control group participants (21.6%) (p = 0.044) (Koivusalo et al., 2016).

Sun and Zhao (2016) performed a quasi-experimental study to assess the impact of a lifestyle intervention on the incidence of GDM and gestational weight gain among obese and overweight women early in the course of their pregnancy. The investigators found that early pregnancy lifestyle intervention was helpful in decreasing the incidence of GDM. In this study, 74 women 8–12 weeks were divided between control (n = 37) and intervention groups (n = 37). The intervention group was provided with counseling on diet, exercise, and weight gain. Moreover, participants received weekly feedback from the research nurse. Throughout the study, the participants were encouraged to identify the factors that helped or hindered their successful implementation of lifestyle modification. The control group only received only usual antenatal care. In the study, GDM was diagnosed in nine of the intervention group and 19 of the control group. Also, chi-square testing indicated that women in the intervention group had a lower incidence of GDM (28.1%) than the women in the control group (55.9%) (p = 0.023) (Sun & Zhao, 2016).

Wang, Ma, and Yang (2015) examined a lifestyle intervention for the prevention of GDM and found lifestyle interventions to be efficacious in reducing the prevalence of GDM when implemented from the beginning of the pregnancy. In this study, 1664 pregnant women with at least one risk factor for GDM were sampled and divided between the control group (n = 138) that received routine antenatal care and the intervention group (n = 134) that received a standardized two-step lifestyle intervention. The study found that the incidence of GDM in the intervention group was lower (17.16%, n = 23) as compared to the control group (23.91%, n = 33), although this difference was not statically significant (p = 0.168). Weight gain during the first and second trimesters for the intervention group was lower (first: M = 1.38, SD = 2.34 kg; second: M = 5.51, SD = 2.18 kg) than the control group (respectively: M = 1.41, SD = 2.58 kg;

M = 5.66, *SD* = 2.25 kg); however, there was no significant difference between the groups (first: *p* = 0.905; second: *p* = 0.567) (Wang, Ma, & Yang, 2015).

Critique of Strengths and Weaknesses

Overall, the quality of the evidence of all 21 studies reviewed in this analysis were rated as level I and level II, meaning that they were either of good or high quality based on the John Hopkins Research Appraisal Tool. The reviewed studies included 14 RCTs, most of which had large sample sizes. The purpose, sample, design, measurements, results/conclusions, and recommendations from the research articles were all easily extracted and compiled into a matrix (see Appendix I). That said, some of the non-RCT studies suffered from low sample sizes and provided inconclusive evidence. Studies of lifestyle interventions, diet, and exercise have demonstrated a positive effect for the control and prevention of GDM. Notwithstanding, further studies are needed to support the use of dietary supplements, such as probiotics and myo-inositol, and sleep modification for the control and prevention of GDM. Furthermore, studies related to the effectiveness of probiotics on GDM (e.g., Lindsey et al., 2014) demonstrate conflicting results. Lindsey et al. (2014) fails to demonstrate an effect for probiotics on the difference between glucose metabolism and changes in blood sugar levels among a sample of pregnant women diagnosed with GDM. Therefore, further studies are needed with larger sample sizes to conclusively determine the effectiveness of probiotics on GDM. Although myo-inositol and sleep have been shown to have a positive effect on the prevention and management of GDM, further RCTs with larger sample sizes are needed to provide conclusive evidence.

Summary

Twenty-one articles were selected and appraised using the Johns Hopkins Research Evidence Appraisal Tool (Dearholt & Dang, 2012). Thirteen studies support the use of certain

diets (e.g., Mediterranean or Dash diets), and dietary supplements (including myo-inositol, probiotics, and vitamin D supplementation) in the prevention and management of GDM. The other eight articles support the use of lifestyle modifications (e.g. sleep, physical exercise, yoga), and lifestyle intervention (e.g., counseling) in the prevention of GDM. Some studies suffered from low sample sizes, and hence, further studies are needed with larger sample sizes to conclusively determine the effectiveness of probiotics, myo-inositol, and sleep on GDM.

The Chapter Four will provide a synthesis of the studies that answer the research question, identifies gaps in the research literature, explores the implications of this knowledge for midwifery practice, and offers a number of recommendations for future areas of study.

Chapter IV: Discussion, Implications, and Conclusions

This chapter explores the implications of non-pharmacological measures for the prevention and treatment of GDM in nurse-midwifery practice, and offers a number of recommendations for future research. This chapter will conclude with an attempt to integrate King's theory of nursing with the preventative measures found to be effective for the control of GDM.

Literature Synthesis

The research question for this review is: "what are the non-pharmacological measures to prevent and treat gestational diabetes mellitus"? To answer this research question, 21 scholarly articles have been identified and appraised. Non-pharmacological interventions included for the prevention of GDM in this review include diet (e.g., MED and Dash diet), dietary supplements (e.g., myo-inositol, probiotics, and vitamin D), lifestyle modifications (including physical exercise, yoga, and sleep duration), and lifestyle interventions. Most of the studies in this review focused on interventions for GDM, with there being some overlap with respect to intervention and prevention. These show that these interventions help not only to reduce the prevalence of GDM, but that they help patients to maintain a healthy gestational weight.

Implications for Practice

Nurse-midwives have the opportunity and responsibility to foster maternal well-being by being aware of interventions that are beneficial. The position statement of the ACNM states that nurse-midwives are primary care providers who "are accountable for addressing the majority of health care needs, developing sustained partnerships with patients, and practicing within the context of family and community" (ACNM, 2012, p. 1). Moreover, health promotion, disease prevention, and health education are among the hallmarks of nurse-midwifery (ACNM, 2013).

Therefore, as health care providers, nurse-midwives should be cognizant of the best preventative measures available for their patients.

Lifestyle interventions and GDM prevention are significantly correlated. Moderate individualized lifestyle interventions were shown to reduce the incidence of GDM by 39% in high-risk pregnant women (Koivusalo et al., 2015). These findings can have positive health consequences for both pregnant mother and their child. High blood sugar levels, often observed in patients with GDM, can lead to fetal hyperglycemia. GDM-induced hyperosmolarity is typically treated with diuretics, thus resulting in increased urination. Consequently, sugar levels are higher in the amniotic fluid, which in turn stimulates secretions from the amniotic membrane, potentially leading to an excess of amniotic fluid. Furthermore, hyperglycemia stimulates fetal insulin secretion, potentially resulting in delayed fetal lung maturity, thereby increasing the incidence of neonatal respiratory distress syndrome (Zhang et al., 2015). This review finds that GDM can be prevented and managed in high-risk populations by simple and easily applicable lifestyle interventions. The findings also suggest that individualized lifestyle interventions should be initiated in early pregnancy in high-risk women and continued throughout pregnancy (Koivusalo et al., 2015).

Nutrition therapy is central to the treatment of diabetes and is essential for its prevention and control (Zhang et al., 2015). Healthy diets have shown to reduce diabetes, improve cardiovascular system and overall health (Benson et al., 2011). Moreover, healthy diets have been shown to have a positive effect on insulin sensitivity, resulting from the replacement of saturated and trans fats with unsaturated fats (Benson et al., 2011). Nurse-midwives should educate women on diets that reduce hyperglycemia as a standard feature of early prenatal care. Effective patient education given to women early in pregnancy empowers them to make healthy

choices that not only affect their pregnancy but their life-long wellness as well as that of their families (Bone, 2015).

Educating expectant mothers about weight gain recommendations on the basis of their pre-pregnancy BMI would be helpful as they would know about how much weight they should be gaining. For pregnant women whose pre-pregnancy BMI is <18.5 kg/m^2, a total weight gain of 28–40 pounds is recommended. A total weight gain of 25–35 pounds is recommended for pregnant women whose pre-pregnancy BMI ranges 18.5–24.9 kg/m^2. For pregnant women whose pre-pregnancy BMI is >25 and <30 pounds, the recommended weight gain is 15–25 pounds. While for those who whose pre-pregnancy BMI is ≥30 kg/m^2, a weight gain in the order of 11–20 pounds is recommended (Bone, 2015).

Recommendations for Future Research

Although diet and lifestyle modifications have shown promising results in the prevention of GDM, RCTs with larger sample sizes are needed for more conclusive results. Furthermore, the effectiveness of sleep and dietary supplements (e.g., myo-inositol, probiotics, and vitamin D) in the prevention of GDM are still inconclusive.

Myo-inositol

This review found studies of myo-inositol supplementation for GDM to be helpful in the regulation of plasma glucose levels. However, the findings were not statistically significant. In the future, a larger, multi-ethnic RCT should be conducted to evaluate the effectiveness of myo-inositol supplementation for glycemic control during pregnancy (Cordero et al., 2015; D'Anna et al., 2013; D'Anna et al., 2015).

Probiotics

Studies of the effectiveness of probiotics for preventing GDM have found combined interventions—such as diet, lifestyle changes, and dietary supplements—to be effective in reducing the prevalence of GDM (Dolatkhah et al., 2015). Dolatkhah et al. (2015) suggests that while probiotic studies demonstrate promising results, the investigators recommend larger scale studies in the future. Lindsay et al. (2015) failed to demonstrate the effectiveness of probiotics in reducing GDM. The investigators conclude that the administration of probiotic capsules to women with abnormal glucose tolerance had no impact on glycemic control. Although probiotics did not appear to have an effect on glycemic control during pregnancy, the results of this study showed a subtle positive effect for cholesterol. LDL cholesterol was slightly reduced among the pregnant women treated with probiotics as compared to the placebo control group (Lindsay et al., 2015). However, the results relating to maternal lipids were modest and the study lacked sufficient sample size to detect changes in these parameters following probiotic treatment (Lindsay et al., 2015).

Vitamin D

Arnold et al. (2015) provides modest evidence for the correlation between early maternal 25-hydroxy vitamin D concentrations and the risk of GDM. One weakness in this study is the single measurement of vitamin D, since the single measurement does not allow for time integrated measures reflecting vitamin D status. Other indicators of the biological activity of vitamin D, including vitamin D binding protein and enzymes related to vitamin D, were not measured in the study. Although, this study provided modest evidence for the association between vitamin D and GDM, the study was not conclusive due to the small sample size and limited statistical significance. Therefore, further investigation with larger sample sizes is needed

in the future to assess the association between GDM and vitamin D concentration (Arnold et al., 2015). The study by Zhang et al. (2008) on the association between concentration of vitamin D and GDM has several strengths. The study determined vitamin D concentration using plasma collected in early pregnancy. Pregnant women normally develop GDM during the second or third trimester. Therefore, the relationship between maternal vitamin D concentrations and GDM provides a strong predictor of GDM. Another strength of the study was the high rate of follow up (Zhang et al., 2008). However, a limitation of this study was the single measurement of vitamin D concentrations. A single measurement does not provide a time integrated measure for vitamin D status throughout the entire pregnancy (Zhang et al., 2008). Although the study showed promising result with respect to the association between maternal vitamin D and GDM, due to its relatively small sample size, further large scale prospective studies are needed to confirm the result of this study (Zhang et al., 2008).

Burris et al. (2012) showed a positive relationship between maternal vitamin D concentrations and GDM. The strengths of the study includes its large sample size, and ability to account for dietary factors and physical activities. Some of the flaws of the study, however, include the cross sectional design of the study and the measurement of 25-hydroxy vitamin D levels from the same blood draw for the screening of the one hour glucose load test (Burris et al., 2012). Although, the blood samples were collected before formal diagnosis of GDM, the onset of glucose intolerance is likely to have predated the blood having been draw. Therefore, it is difficult to rule out reverse causation, such as physiologic changes that result from hyperglycemia that might lower 25-hydroxy vitamin D level (Burris et al., 2012).

Although some dietary supplements have shown promising results in the management of GDM, none of the studies in this review discussed the prevention of long-term glucose intolerance or type II diabetes that may result from GDM.

Integration of King's Nursing Theory

This findings of this review attest to the benefits of alternatives to pharmacological interventions for the GDM. In order to successfully implement these alternatives, patients must be actively involved in their own care. King's TGA would help to facilitate the interaction between the provider and the patient. This interaction would help the provider assess the patient and learn about their expectations and goals for the intervention. It would also provide baseline information about the patient's expectations and interest in managing GDM in the absence of pharmacological interventions. This interaction would also help both parties to understand each other, and allow the provider to diagnose the patient's environment and their personal habits, such as diet and exercise. After diagnosis, the provider can develop dietary and exercise goals in collaboration with the patient, these goals being mutually agreed upon by both parties, and allow various natural interventions to be implemented in order to achieve these goal. Throughout the pregnancy, these goals should be evaluated during each visit, and readjusted and implemented accordingly (Caceres, 2015).

The involvement of other family members is crucial in the care of the patient and is consistent with the promotion of the King's theory of patient-family-centered care, encouraging collaboration among health care professionals, the patient, and their family. If a patient at risk for the development of GDM presents for a prenatal visit, King's theory suggests that family members should be involved to encourage the patient to be physically active and help with the dietary plan. It should be mutually understood that the family member and the provider will help

the patient to adhere to the agreed dietary plan. Patients are more likely to be satisfied with their care and the treatment plan is more likely to be successful with the involvement of other family members. Therefore, according to King's TGA, the involvement of other family members in the treatment of GDM is beneficial for the nurse-midwife, the patient, and the entire family.

The review is focused on empowering the patients by making them aware about the various natural therapy options and alternatives to pharmacological interventions that are available for the prevention and treatment of GDM. In order to successfully implement these alternatives, patients are expected to be actively involved in their own care (Leon-Demare et al., 2015). Due to King's TGA having an emphasis on patient-family-centered care, close nurse-patient relationships, and emphasis on patient self-care, this model would likely facilitate the successful prevention and treatment of GDM through non-pharmacological therapies. Consequently, this theory provides an ideal conceptual framework for this review.

Conclusion

This review has identified a number of efficacious non-pharmacological interventions for the prevention and management of GDM. Using the Johns Hopkins Research Evidence Appraisal Tool, 21 scholarly articles were analyzed to identify various non-pharmacological interventions of significance. The review found diets, such as the MED and Dash diet; dietary supplements, including myo-inositol, probiotics, and vitamin D; lifestyle modifications, such as physical exercise, yoga, sleep duration; and lifestyle interventions show promising results in the prevention and management of GDM.

Nurse-midwives are in an ideal position to foster maternal well-being and to provide various treatment options that are beneficial for pregnant women. GDM can have adverse effects on the health of both mother and baby, affecting 15% of pregnancies worldwide, and 2–10% of

pregnancies in the US. Therefore, nurse-midwives should remain up-to-date on effective interventions, as well as current research trends in relation to GDM to safeguard the health of both the pregnant mother and her baby. Nurse-midwives should be well-informed, not only of the interventions for GDM, but the use King's TGA in order to implement these interventions, thus facilitating the achievement of the goal of preventing and managing GDM. If mothers are hesitant to use pharmaceutical therapies and prefer other alternatives, then the findings of this review would be of use to nurse-midwives in order to recommend appropriate non-pharmacological interventions for GDM. The most important contribution of the review rests in the identification of various natural interventions and their effectiveness in the prevention and treatment of GDM.

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Appendix I

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Anjana, R. M., Sudha, V., Lakshmipriya, N., Anitha, C., Unnikrishnan, R., Bhavadharini, B., & ... Mohan, V. (2016). Physical activity patterns and gestational diabetes outcomes - The wings project. *Diabetes Research & Clinical Practice, 116*(2016). doi:10.1016/j.diabres.2016.04.041	To assess the effectiveness of exercise on blood glucose level and pregnancy outcome among the patients with gestational diabetes mellitus.	1083 pregnant women included in the study were divided into GDM group (*n* = 247), and non-GDM group (*n* = 836).	Case control study.	Physical activity questionnaire and pedometer to measure the physical activity. Plasma glucose and glycated haemoglobin (HbA1c) measured.	Women with GDM were significantly more sedentary compared to those without GDM (86.2 vs. 61.2%, *p* = 0.001). Increase in physical activity also significantly decrease the blood glucose levels (*p* = 0.001). Physical activities are associated with improved glycemic control.	Further larger randomized control trails in other low and middle income countries around the world.	Level I - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Koivusalo, S. B., Rono, K., Klemetti, M. M., Roine, R. P., Lindstrom, J., Erkkola, M., & ... Pöyhönen-Alho, M. (2016). Gestational diabetes mellitus can be prevented by lifestyle intervention: The Finnish gestational diabetes prevention study (RADIEL): a randomized controlled trial. *Diabetes Care, 39(*1), 24-30. doi:10.2337/dc15-0511	To assess the prevention of gestational diabetes mellitus for the patient at higher risk by a moderate lifestyle intervention.	293 women meeting the following criteria were randomized either to intervention (n = 155) or control groups (n = 138): <20 weeks pregnant, history of GDM, and pre-pregnancy weight ≥30 kg/m^2	Randomized control trial. The intervention group received individualized counseling on diet, physical activity, and weight control from trained nurses, and also had one group meeting with a dietician. The control group received only standard antenatal care.	The diagnosis of gestational diabetes mellitus was done on the basis of 75 g, 2 hr oral glucose tolerance test at 24-28 weeks of gestation.	GDM was diagnosed in 20 intervention group participants (13.9%) and 27 control group participants (21.6%) (p = 0.044). In intervention group, the 2 hour glucose value increased by 0.54 mmol/L from the baseline to second trimester and in control group by 0.55 mmol/L. The intervention group increased their physical activity and improved their dietary quality during pregnancy which indicates a healthier direction. With combined moderate physical activity and diet, the overall incidence of GDM was reduced by 30%. However, the control group participants did not increase their physical activity or improve the dietary quality in significant manner.	The study was only performed on white population. However, it may be reasonable to generalize as the study protocol was straightforward and can be implemented in other ethnic groups. Also, the larger sample size is needed to see the effect on maternal and neonatal outcomes.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Izadi, V., Tehrani, H., Haghighatdoost, F., Dehghan, A., Surkan, J, P., & Azadbakht, L. (2016). Adherence to the Dash and Mediterranean diets is associated with decreased risk for gestational diabetes mellitus. *Nutrition, 32*(2016), 1092-1096. doi: 10.1016/j.nut.2016.03.006	To evaluate the effectiveness of Dash and MED diets for preventing gestational diabetes.	Two groups of pregnant women were studied: one group with GDM (*n* = 200) and the other without GDM (*n* = 260)	Case control hospital-based study.	Food records were analyzed with nutritionist IV software modified for Iranian foods. Dash score was calculated using Fung and MED score was calculated using Trichopoulou methods. Tertiles of Dash and MED dietary pattern scores was used.	MED diet is negatively related to fasting blood glucose levels, hemoglobin A1C, and serum triacylglycerol concentrations. The total serum cholesterol level was lower in the third tertile of the MED diet group. Participants in the highest tertile of the MED diet group had an 80% lower risk for GDM as compared with those in the lowest tertile (*p* = 0.006). Adherence to the Dash diet was associated with 71% lower risk of GDM It is indicated that adherence to Dash and MED diets was associated with decreased risk of GDM.	Larger cohort studies would help to provide a stronger evidence of the impact of MED and Dash diets on GDM. Also, the study is limited to only 3 24 hour dietary records to assess dietary intake. A more comprehensive data keeping may provide stronger evidence. Also, further studies are needed in the countries without the above diets to confirm these results.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Sununta, Y., Sasitorn, P., & Thitiporn, I. (2014). The effects of mindfulness eating and yoga exercise on blood sugar levels of pregnant women with gestational diabetes mellitus. *Applied Nursing Research, 27*(4), 227-230. doi:10.1016/j.apnr.2014.02.002	To assess the effect of mindfulness eating and yoga exercise on the blood sugar levels among pregnant Thai women with GDM.	A sample of 180 women with GDM were randomized to intervention (n = 90) and control groups (n = 90).	Randomized controlled trials.	Participants in intervention group participated in two sessions of mindfulness eating and yoga session in class, and more than 80% of sessions were practiced in their home. The measurements of blood sugar were by capillary fasting plasma glucose, 2h postprandial blood glucose and hemoglobin A1c.	The women with GDM in the intervention group had significantly lower fasting blood glucose levels (M = 83.39, SD = 17.69 mg/dL), postprandial blood glucose levels (M = 105.67, SD = 12.93 mg/dL), and A1C levels (M = 5.23%, SD = 0.72 mg/dL) than those in the control group (respectively: M = 85.85, SD = 17.94 mg/dL, p = 0.012; M = 112.36, SD = 13.15 mg/dL, p = 0.001, $p <$ 0.05; M = 5.68%, SD = 0.68, p = 0.038) Mindfulness eating and yoga exercise were effective for glycemic control among pregnant women with GDM.	Mindfulness eating and yoga exercise were prescribed to the patient to follow through themselves in their home instead of as a group intervention study at the research center. Therefore, further studies are needed to compare the effectiveness of mindfulness eating and yoga exercise on GDM between practicing alone at home or in a group setting.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
D'Anna, R., Scilipoti, A., Giordano, D., Caruso, C., Cannata, M. L., Interdonato, M. L., & ... Di Benedetto, A. (2013). myo-Inositol supplementation and onset of gestational diabetes mellitus in pregnant women with a family history of type 2 diabetes: a prospective, randomized, placebo-controlled study. *Diabetes Care, 36*(4), 854-857. doi: 10.2337/dc12-1371	To check the effectiveness of myo-inositol supplementation in reducing the onset of gestational diabetes among the pregnant women with family history of type 2 diabetes mellitus.	220 pregnant Caucasian women were included. *n* = 110 in the intervention group were treated with 2 g myo-inositol plus 200 mui g folic acid twice a day, whereas *n* = 110 in the placebo group were only treated with 200 mui g folic acid twice daily.	Prospective, randomized, open label, and placebo controlled study.	The diagnosis of diabetes was performed with 75-g, 2-h glucose tolerance test. Statistical analysis was done with SPSS v17. Student t-test Fisher exact test and Pearson X2 tests were used for analysis.	The study showed a significant reduction in the incidence of GDM in the myo-inositol group (6%) as compared to the placebo control group (15.3%) (p = 0.04). Moreover, there was a difference in mean birth weight between the groups (3111v 3273 g). 7 fetuses in placebo group weigh > 4000 g and there were none in the control group. The study supports the involvement of inositol in the mechanisms of glycemic control. It also concluded that inositolphosphogl may play a role not only in glycemic control, but also in the fetal growth of GDM women.	Larger studies are required to confirm the effect of myo-inositol supplementation in prevention of GDM.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Sun, Y., & Zhao, H. (2015). The effectiveness of lifestyle intervention in early pregnancy to prevent gestational diabetes mellitus in chinese overweight and obese women: a quasi-experimental study. Applied *Nursing Research, 30*(2016). Doi: 10.1016/j.apnr.2015.10.006	To assess the impact of lifestyle intervention in early pregnancy on the reduction of the incidence of GDM and gestational weight gain among Chinese overweight and obese pregnant women.	74 women 8–12 weeks were divided between control (*n* = 37) and intervention groups (*n* = 37).	Quasi-experimental study. Convenience sampling.	At 24-30 weeks glucose challenge test was performed on all and oral glucose tolerance test was performed on women with glucose value > 7.8 mmol/l. GDM diagnosis was made according to IADPSG criteria. The weight gain was calculated as the weight difference between weight at 28 weeks and pre pregnancy.	GDM was diagnosed in nine of the intervention group and 19 of the control group. Also, chi-square testing indicated that women in the intervention group had a lower incidence of GDM (28.1%) than the women in the control group (55.9%) (*p* = 0.023) The gestational weight gain at the end of 28 weeks was significantly higher among control group (10.08 kg) as compared to intervention group (6.86 kg) (p = 0.001). Lifestyle intervention during early pregnancy is effective in decreasing the incidence of gestational diabetes and also decreasing the excessive maternal weight gain at the end of second trimester in overweight and obese Chinese women.	Further research should be performed with a large sample size. The patients should be recruited from different hospital and in randomized method. In this research the samples were only recruited from a single hospital and not in a randomized method. Moreover, self-reporting of pre pregnancy weight should be replaced by reliable method.	Level II - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Cordero, Y., Mottola, M. F., Vargas, J., Blanco, M., & Barakat, R. (2015). Exercise is associated with a reduction in gestational diabetes mellitus. *Medicine & Science In Sports & Exercise, 47*(7), 1328-1333. doi:10.1249/MSS.0000000000000547	To assess the effectiveness of a maternal exercise program (land/aquatic activities, both aerobic and muscular conditioning) in preventing GDM.	257 pregnant women were randomized either to an intervention group (n = 101) with physical exercises or to a sedentary control group (n = 156)	Randomized control trial.	50 gram maternal glucose screen at 24-28 week of gestation, and glucose level was determined 1 hour after a 50 -g load of glucose administration orally. The screen test was considered positive when the values are equal or greater than 140 mg/dl. Statistical analysis such as t-test, X-test, etc. were performed with SPSS v20.	There were no differences for the 50-g maternal glucose screening values between the groups. However, the glucose values corresponding to OGTT at 3 hours showed that interventional group had lower values blood sugar level compared to control group. The study found significant difference between the prevalence of GDM between the intervention (1%, n = 1) and control groups (8.8%, n = 13) (p = 0.009). Overall, physical inactivity is associated with the risk of glucose intolerance, and physical activity is associated with better response to glucose metabolism.	There was no nutrition analysis performed, in the study. All the women were exposed to the same standard care that emphasizes healthy eating and healthy lifestyle. Therefore, future studies need to have nutritional study.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Zhang, C., Qiu, C., Hu, F. B., David, R. M., van Dam, R. M., Bralley, A., & Williams, M. A. (2008). Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes Mellitus. *PLoS ONE*, *3*(11). doi: 10.1371/journal.pone.0003753	To assess the effectiveness of vitamin D in maintaining glucose homeostasis during gestational diabetes.	Total 953 pregnant women were selected with 57 women, who developed GDM as intervention group, and 114 pregnant women without GDM as control.	Case control study.	Pregnant women were screened at 24-28 weeks gestation using 50 grams 1- hour oral glucose challenge test. Plasma 25-(OH) D concentrations were measured using DiaSorin immuneassay reagents.	Pregnant women who developed GDM had vitamin D concentrations significantly lower than control (24.2 vs. 30.1 ng/ml, p <0.001). The study suggest that maternal vitamin D deficiency in early pregnancy is significantly associated with an elevated risk of GDM.	Further longitudinal studies with serial measurements of maternal plasma 25-(OH) D concentrations are needed. Larger sample size and inclusion of minority group would give the better result.	Level I - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Asemi, Z., Samimi, M., Tabassi, Z., Sabihi, S., & Esmaillzadeh, A. (2013). A randomized controlled clinical trial investigating the effect of Dash diet on insulin resistance, inflammation, and oxidative stress in gestational diabetes. *Nutrition, 29*(4), 619-624. doi:10.1016/j.nut.2012.11.020	To investigate the effects of the Dash diet on insulin resistance, serum high sensitivity C-reactive protein and biomarkers of oxidative stress among pregnant women with GDM.	32 pregnant women diagnosed with GDM at 24 to 28 week gestation were randomized into Dash diet group (n = 16) and control group (n = 16).	Randomized control trial.	After 4 weeks of intervention, anthropometric measure, maternal weight, fasting blood sugar, serum insulin level and insulin resistance, serum hs-CRP levels, and plasma total antioxidant capacity were assessed.	In this study mean age, pre-pregnancy weight, and BMI were not statistically different between two groups. However, the Dash diet group had a lower FPG (-7.62 mg/dl) as compared to the control group (3.68 mg/dl) (p = 0.02). The Dash diet group also had lower serum insulin levels (-2.62 uIU/ml) as compared to the control group (4.32 uIU/ml) (p = 0.03) Consumption of Dash diet in pregnant women with GDM had beneficial effects on FPG, serum insulin levels, HOMA-IR score, plasma TAC, and total GSH levels.	The effects of dietary pattern on pregnancy outcomes should be studied further with larger sample size in the future studies.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
DAnna, R., Di Benedetto, A., Scilipoti, A., Santamaria, A., Interdonato, M. L., Petrella, E., & ... D'Anna, R. (2015). Myo-inositol supplementation for prevention of gestational diabetes in obese pregnant women: A randomized controlled trial. *Obstetrics & Gynecology, 126*(2). doi:10.1097/AOG.0000000000000958	To evaluate the effectiveness of myo-inositol supplementation in preventing gestational diabetes among obese pregnant women.	Two groups of pregnant women with GDM: myo-inositol group (n = 110) and placebo group (n = 110).	Open-label randomized trial.	Oral glucose tolerance test (OGTT)	The study showed the rate of GDM was significantly reduced in the myo-inositol group (14%) as compared with the control group (33.6%) (p = 0.001). Furthermore, the study found that the women who were treated with myo-inositol showed a significantly greater reduction in homeostasis model assessment of insulin resistance (M = -1.0, SD = 3.1) as compared with the women in the control group (M = 0.1, SD = 31.8) (p = 0.048). Myo-Inositol supplementation, started in the first trimester, in obese pregnant women seems to reduce the incidence in GDM through a reduction of insulin resistance.	Future studies with randomized control trial and larger sample size without dropouts.	Level I - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Burris, H. H., Rifas-Shiman, S. L., Kleinman, K., Litonjua, A. A., Huh, S. Y., Rich-Edwards, J. W., … Gillman, M. W. (2012). Vitamin D deficiency in pregnancy and gestational diabetes. *American Journal of Obstetrics and Gynecology, 207*(3). Doi:10.1016/j.ajog.2012.05.022	To assess the association between second trimester maternal plasma vitamin D level and gestational diabetes.	1314 pregnant women, participants of Project Viva, a birth cohort study, were included.	Prospective cohort study.	At 26-28 weeks gestation Vitamin D, vitamin D2 and vitamin D3 levels were measured of all pregnant women. GDM clinical data were recorded via 1 hour GTT, and if patient fails 1 hour, 3 hour GTT was performed.	68 women met the criteria for GDM. The study showed that second trimester vitamin D levels were inversely associated with glucose levels (p <0.01). Low 25 (OH) D level may be associated with increased risk of GDM.	Further studies with randomized control trials will be needed to further support that vitamin D supplementation affects GDM risk.	Level II - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Laitinen, K., Poussa, T., & Isolauri, E. (2009). Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial. *British Journal Of Nutrition, 101*(11), 1679-1687. doi:10.1017/S0007114508111461	To examine the association between probiotic supplementation in glucose metabolism in normoglycemiac pregnant women.	256 women during their first trimester were randomized into three groups to receive both a special diet and probiotics (n = 85), diet and placebo (n = 86), and placebo only (n = 85).	Randomized control trial.	Plasma glucose concentration was measured and blood glycated Hb A1C, and serum insulin concentration were measured among all participants.	The study found blood glucose concentrations were lowest in the diet/probiotics group (M = 4.45 mmol/l) as compared to the diet/placebo (M = 4.60 mmol/l), and placebo groups (M = 4.56 mmol/l) (p = 0.025). The study demonstrated that improved blood glucose control can be achieved by dietary counseling with probiotics even in normoglycemic population.	None	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Dolatkhah, N., Hajifaraji, M., Abbasalizadeh, F., Aghamohammadzadeh, N., Mehrabi, Y., Abbasi, M. M., & Mesgari Abbasi, M. (2015). Is there a value for probiotic supplements in gestational diabetes mellitus? a randomized clinical trial. *Journal Of Health, Population & Nutrition, 331*(8). doi:10.1186/s41043-015-0034-9	To assess the effect of a probiotic supplement capsule on glucose metabolism and weight change in women with newly diagnosed GDM.	64 pregnant women were randomized to receive either probiotic supplementation (n = 32) or placebo capsules (n = 32) along with dietary advice for eight consecutive weeks.	Double blind placebo controlled randomized clinical trial. Intervention group received the probiotic capsule, and control group received placebo capsules. Similar diets were provided to all subjects in the study.	Fating blood sugar were obtained from all participants before and after the intervention. Data was analyzed using SPSS v22.	The insulin resistance index in the probiotic group decreased significantly (6.74%) as compared to the placebo group, which showed an increase in insulin resistance (6.45%) ($p < 0.03$). The pattern of weight gain was similar for both groups until six weeks; in the last two weeks of the study, weight gain in the probiotic group was significantly lower ($M = 0.74$, $SD = 0.14$) as compared to the placebo group ($M = 1.22$, $SD = 0.11$) ($p = 0.01$). Hence, probiotic supplement affect glucose metabolism and weight gain among pregnant women with GDM.	The findings needs to be confirmed in other settings before a therapeutic value could be approved.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Corrado, F., D'Anna, R., Di Vieste, G., Giordano, D., Pintaudi, B., Santamaria, A., & Di Benedetto, A. (2011). The effect of myoinositol supplementation on insulin resistance in patients with gestational diabetes. *Diabetic Medicine, 28*(8), 972-975. doi:10.1111/j.1464-5491.2011.03284.x	To test that myoinositol supplementation will improve insulin resistance in patients with gestational diabetes.	Sixty nine patients with gestational diabetes were randomly assigned to study group that received myo inositol as tablet and folic acid (n = 24) and control group that received folic acid only (n = 45) for 8 weeks.	Randomized, controlled trial with open label.	The diagnosed oral glucose tolerance test was performed at the diagnostic and after 8 weeks. Homeostasis model assessment of insulin resistance and adiponectin were assayed. Statistical analysis was performed with SPSS v17.	There were three women in the study group and nine in the control group who required insulin treatment. Fasting glucose and insulin, and consequently homeostasis model assessment of insulin resistance decreased in both groups (50% in the study group vs. 29% in the control group), but the decline in the study group was significantly greater than that in the control group (p = 0.0001). Overall, myoinositol improves insulin resistance in patients with gestational diabetes.	Further research is required with a larger sample and inclusion of other races.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Lindsay, K. L., Brennan, L., Kennelly, M. A., Maguire, O. C., Smith, T., Curran, S., & ... McAuliffe, F. M. (2015). Impact of probiotics in women with gestational diabetes mellitus on metabolic health: a randomized controlled trial. *American Journal Of Obstetrics & Gynecology, 212*(4). doi:10.1016/j.ajog.2015.02.008	To investigate the effects of probiotic capsule intervention on maternal metabolic parameters and pregnancy outcome among pregnant women with gestational diabetes mellitus.	149 women with GDM were randomized in to two groups and provided with probiotic capsules, intervention group (n = 74), and placebo capsules, control group (n = 75).	Randomized control trial.	Fasting blood sugar were drawn at the beginning of the study, and 4-6 weeks after starting the capsule for analysis of glucose, insulin, c-peptide and lipids.	Post-fasting glucose levels were the same for both intervention (M = 4.65, SD = 0.49 mMol/L) and placebo groups (M = 4.65, SD = 0.53 mMol/L) (p = 0.373) A probiotic capsule intervention among women with abnormal glucose tolerance had no impact on glycemic control.	Further investigation and research on probiotic supplementation is required for conclusive result.	Level I - High.

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Twedt, R., Bradley, M., Deiseroth, D., Althouse, A., & Facco, F. (2015). Sleep duration and blood glucose control in women with gestational diabetes mellitus. *Obstetrics & Gynecology, 126*(2), 326-331. doi:10.1097/AOG.0000000000000959	To assess the relationship between sleep duration and glucose control in GDM patients.	45 women diagnosed with GDM	Prospective cohort study.	Participants were asked to follow recommended diet and measure their fasting and 1- hour postprandial glucose values for 1 week. Also, participants wore an actigraph to objectively assess sleep and completed a sleep diary for 7 days immediately after their GDM education class.	The study showed that an one hour increase in sleep resulted in a statistically significant reduction in fasting glucose ($p = 0.03$), post-lunch glucose ($p = 0.03$), and post-dinner glucose ($p = 0.001$). It was found that short sleep durations are associated with worsened glucose control in women with gestational diabetes. Educating women on healthy sleep and screening sleep disorder may have a role in optimizing blood glucose in GDM.	Further studies with larger sample size to study the relationship between the duration of sleep and glucose control in GDM patient.	Level II - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Arnold, D. L., Enquobahrie, D. A., Qiu, C., Huang, J., Grote, N., VanderStoep, A., & Williams, M. A. (2015). Early pregnancy maternal vitamin D concentrations and risk of gestational diabetes mellitus. *Paediatric & Perinatal Epidemiology, 29*(3), 200-210. doi:10.1111/ppe.12182	To examine associations of vitamin D with gestational diabetes mellitus.	Control group with GDM (*n* = 135) and an intervention group without GDM (*n* = 517)	Prospective nested case-cohort study.	During early pregnancy (16 weeks) vitamin D concentrations were measured in maternal serum using liquid chromatography-tandem mass spectroscopy. GDM was diagnosed according to the American Diabetes Association guidelines.	The study showed that women with GDM had lower levels of vitamin D (*M* = 27.3, *SD* = 8.7 ng/mL) as compared to those without GDM (*M* = 29.3, *SD* = 8.3 ng/mL) (*p* = 0.01). This study demonstrated a 14% reduction in the incidence of GDM with a 5 ng/mL increase of vitamin D supplementation in GDM patients. Furthermore, women with total vitamin D deficiency had a 1.97 fold increased risk for GDM (95% CI 1.12, 3.47) Early pregnancy vitamin D status, particularly vitamin D3, is inversely associated with GDM risk.	Additional studies are needed to better understand the association between maternal vitamin D deficiency and GDM.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Rawal, S., Hinkle, S. N., Zhu, Y., Albert, P. S., & Zhang, C. (2016). A longitudinal study of sleep duration in pregnancy and subsequent risk of gestational diabetes: findings from a prospective, multiracial cohort. *Am J Obstet Gynecol* (2016). doi: 10.1016/j.ajog.2016.11.1051	To examine the trimester-specific association between typical sleep duration in pregnancy and subsequent risk of gestational diabetes.	2581 pregnant women who reported their typical sleep duration and napping frequency in the first and second trimester. Diagnosis of GDM (*n* =107; 4.1%) was based on medical record.	The prospectiv e study was conducted on the Eunice Kennedy Shriver National Institute of Child Health and Human Developm ent Singleton cohort (2009 through 2013)	GDM diagnosis was abstracted from medical records (*n* = 107). The diagnoses was based on either the oral glucose tolerance test, using the Carpenter and Coustan diagnostic criteria or indications of medication treated GDM on the hospital charge diagnosis (*n* = 12).	Sleeping duration in the second but not first trimester was significantly related to risk of GDM. Among nonobese but not obese women, both sleeping >8 hr and <8 hr were significantly related to risk of GDM: 5-6 hours sleep (relative risk 2.52%), 7 hours (2.01%), >10 hour (2.17%). Significant effect modification by napping frequency was also observed. Positive association between reduced sleep (5-7 hr) and GDM was observed among women who rarely napped (risk 2.48%). Overall, the study provide an important contribution to the understanding of the link between sleep duration and GDM risk.	Future studies that assess sleep quality and include objective measures of nocturnal and daytime sleep duration are needed to extend the findings.	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Zhang, Q., Cheng, Y., He, M., Li, T., Ma, Z., & Cheng, H. (2016). Effect of various doses of vitamin D supplementation on pregnant women with gestational diabetes mellitus: A randomized controlled trial. *Experimental and Therapeutic Medicine, 12*(3), 1889–1895. doi: 10.3892/etm.2016.3515	To assess the effectiveness of various doses of vitamin D supplementation on pregnant women with gestational diabetes mellitus.	133 pregnant women with GDM were randomized in four groups: control group (n = 20) received a placebo, while the other three groups received different amounts of vitamin D: low dose (200 IU, n = 38), medium dose (2000 IU daily for 25 days to 50000 IU in total, n = 38), and high dose (4000 IU daily and 50,000 IU every 2 weeks, n = 37).	Randomized double blind, controlled clinical trial.	Serum 25 (OH) D concentrations were assayed using a commercial ELISA kit. Further, blood sample for the measurement of fasting plasma glucose (FPG), insulin.	The study found that insulin, HOMA, and total cholesterol were significantly reduced in the high dose vitamin D supplementation group (p = 0.01). The study supports high dose vitamin D supplementation for improving insulin resistance in patients with GDM	None	Level I - High

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Karamanos, B., Thanopoulou, A., Anastasiou, E., Assaad-Khalil, S., Albache, N., Bachaoui, M., & ... Savona-Ventura, C. (2014). Relation of the Mediterranean diet with the incidence of gestational diabetes. *European Journal Of Clinical Nutrition, 68*(1), 8-13. doi:10.1038/ejcn.2013.177	To explore a possible relationship between the incidence of GDM and the MED diet pattern of eating.	1076 pregnant women were studied.	Prospective, observational, non-interventional, and multi-center study performed in 10 centers, in 10 Mediterranean countries.	An OGTT was performed during the 24-32 weeks with 75 g of glucose. Dietary questionnaire and dietary habits were assessed and MED diet index (MDI) was computed.	The study showed that the incidence of GDM was lower in subjects with better adherence to the MED diet (8%) as compared to those with poor adherence (12%) ($p = 0.03$). Adherence to a MedDiet pattern of eating is associated with lower incidence of GDM and better degree of glucose tolerance, even in women without GDM.	There were relatively small number of population from each country. A larger collective analysis of data from various population is necessary in future studies.	Level II - Good

Citation	Purpose	Sample	Design	Measurement	Results/ Conclusions	Recommendation	Level & Quality
Wang, S., Ma, J., & Yang, H. (2015). Lifestyle intervention for gestational diabetes mellitus prevention: a cluster-randomized controlled study. *Chronic Disease & Translational Medicine, 1*(2015). doi: 10.1016/j.cdtm.2015.09.001	To examine whether GDM can be prevented by early trimester lifestyle counseling in the high-risk population.	1664 pregnant women with at least one risk factor for GDM were sampled and divided between the control group (n = 138) that received routine antenatal care and the intervention group (n = 134) that received a standardized two-step lifestyle intervention.	Cluster randomized control study.	Lifestyle interventions such as diet, exercise, counseling and measurement of serum blood glucose level.	The study found that the incidence of GDM in the intervention group was lower (17.16%, n = 23) as compared to the control group (23.91%, n = 33), although this difference was not statically significant (p = 0.168). Weight gain during the first and second trimesters for the intervention group was lower (first: M = 1.38, SD = 2.34 kg; second: M = 5.51, SD = 2.18 kg) than the control group (respectively: M = 1.41, SD = 2.58 kg; M = 5.66, SD = 2.25 kg); however, there was no significant difference between the groups (first: p = 0.905; second: p = 0.567). Although there was no statistically significant difference, the positive rate of GDM could be reduced by a certain amount of lifestyle intervention from the beginning of pregnancy.	Effective intervention should be explored for the high-risk pregnant women.	Level I - High