Investigating Associations between Consumption of Unprocessed and Ultra Processed Foods and Maternal and Neonatal Health Outcomes—Secondary Outcomes of LIFT Trial

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ABSTRACT

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The ultra-processing of food has become a much more important aspect of dietary patterns and dietary quality in terms of its impact on body weight, diet related diseases, health, and well-being in the past decades. NOVA is a set of guidelines developed that classifies diet quality by degree of food processing. The NOVA guidelines distinguish four categories: unprocessed /minimally processed foods; culinary ingredients; processed foods; and ultra-processed foods. Numerous studies have found an association of ultra-processed foods and health conditions such as obesity and metabolic syndrome. This study analyzed the associations between maternal diet quality as measured by NOVA and maternal anthropometric and neonatal body composition outcomes. The optimal method of nutrition intervention and education for this special population remains unknown; using NOVA may provide researchers with a different lens to assess diet quality and health care professionals with additional vocabulary to convey more tailored messages regarding optimal nutrition strategies for mother and offspring. Using data collected from a large randomized controlled intervention trial at pre and post intervention, this study aimed to compare the NOVA guidelines assessment of maternal diet quality to the parent study assessment of diet quality, the Healthy Eating Index (HEI), using statistical correlations. Secondly, this study aimed to look at the relationship of ultra-processed food intake to the maternal gestational weight gain experience using a logistic regression. Thirdly, this dissertation aimed to explore the relationship between maternal ultra-processed food intake and neonatal lean

mass as measured by quantitative magnetic resonance (QMR) and fat free mass as measured by air displacement plethysmography (ADP: PEAPOD).

In terms of maternal outcomes, the study found that NOVA and HEI were significantly correlated at pre intervention but not at post intervention. The odds of gaining excessive gestational weight decreased as maternal ultra-processed food intake increased - which was not in the hypothesized direction - when using study participant data. However, the odds of gaining excessive gestational weight increased as maternal ultra-processed food intake increased - which was in the hypothesized direction - when using the Institute of Medicine weight gain recommendations. Also, while obesity did not predict excessive gestational weight gain, those with obesity ultra-processed food intake did predict gestational weight gain. These various inconsistencies are likely due to the instability of the dietary intake data because only one 24 - hour dietary recall was obtained from mother. In addition, the mothers' diets were very healthy to begin with, where ultra-processed food intake formed about 45% of calories both pre and post intervention, when the national average is 57%. Race was also significant predictors of gestational weight gain for the mothers. Being non-white significantly increased the odds of gaining excessively as did the interaction of having obesity and eating more ultra-processed foods.

In terms of neonatal outcomes, findings from this study suggest that length and fat mass are significant predictors of lean mass in neonates. In terms of the impact of maternal ultra-processed food intake, the higher the consumption of ultra-processed food, the greater the neonatal lean mass, which this was not in the hypothesized direction. However, the association was minimal with very small beta weights and regression line, when plotted was quite flat, so that the finding is not clinically meaningful.

It remains important to know whether maternal ultra-processed food intake influences gestational weight gain and the body composition of the neonate. Thus, future research should include using similar data analyses on a population with a more nationally representative diet, a larger sample size, and a more robust measure of dietary intake such as three 24-hour recalls. Given that a similar recent study found ultra-processed food to be highly predictive of maternal and neonatal outcomes, and many other studies have demonstrated that ultra-processed food is related to several health conditions in many countries that this study did not measure, it seems prudent for healthcare providers to take advantage of prenatal visits as a window of opportunity to encourage the consumption of unprocessed and minimally foods and help women make informed decisions regarding ultra-processed foods.

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LIST OF ACRONYMS

ADP: Air Displacement Plethysmography

BMI: Body Mass Index

BW: Body Weight

DPP: Diabetes Prevention Program

FM: Fat Mass

FFM: Fat-Free Mass

GDM: Gestational Diabetes Mellitus

GI: Glycemic Index

GWG: Gestational Weight Gain

HEI: Healthy Eating Index

IOM: Institute of Medicine

LGA: Large for Gestational Age

LI: Lifestyle Intervention

LIFT: Lifestyle Intervention for Two

LIFE-Moms: Lifestyle Interventions for Expectant Moms

Look AHEAD: Action in Health for Diabetes

PEI: Percentage of Energy Intake

PFW: Percentage of Food Wight

QMR: Quantitative Magnetic Resonance

SES: Socioeconomic Status

SGA: Small for Gestational Age

SOFAAS: Solid Fats, Alcohol and Added Sugar

UC: Usual Care

UPFD: Ultra-processed food and drink

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Dedication

To my brother, Thomas Patrick Whyte

(January 27, 1959–May 31, 2013), 25 years my senior,

who showed me what hard work and compassion looked like in action and

who reminded me every morning from kindergarten on that

I'd "better get letters after your name if you want to be someone in this world, pup."

Chapter I

BACKGROUND, SIGNIFICANCE, AND AIMS

Introduction: The Global Problem of Maternal Obesity and Gestational Weight Gain

Obesity is well documented in the literature as being positively associated with shorter life expectancy and multiple co-morbidities.[1] Several studies have shown that excessive weight gain during pregnancy is a strong predictor of postpartum weight retention, which may contribute to obesity in women of childbearing age who engage in a cycle of weight gain.[2] Indeed, studies have shown that one third of pregnant women tend to gain excessive weight during their pregnancy.[2] Moreover, the economic burden of maternal overweight, gestational diabetes mellitus (GDM), and related macrosomia is significant. One study using US-costing data estimated the annual cost of maternal overweight, GDM, and related macrosomia to exceed $1.8 billion; this estimate only considered health costs during the perinatal period, and not long-term consequences such as offspring health.[3] Still, while obesity is widely recognized as a global issue, obesity in women of child-bearing age is often overlooked. Consequently, there is a paucity of information and best-practice strategies related to weight management delivered to this population at points of care, such as obstetrician/gynecologist offices.

The Institute of Medicine (IOM) has provided recommendations for gestational weight gain (GWG) based on pre-pregnancy body mass index (BMI). For normal weight women (BMI: 18.5-24.9), the IOM recommends a weight gain of 11.4 to 15.9 kg during pregnancy, and these recommended targets decrease as BMI increases. For overweight women (BMI: 25.0-29.9), weight gain drops to between 6.8 and 11.4 kg; for obese women, (BMI: $\geq$ 30), the IOM recommended even lower weight gain, to 5.0 to 9.0 kg.[4] Research has suggested that weight gain within IOM recommendations is associated with healthy fetal and maternal outcomes.[5] Despite

the evidence and the wide dissemination of these recommendations by the IOM and other public health and scientific communities, approximately 55% of normal weight women and 65% of overweight/obese women continue to gain weight in excess of these guidelines. In standard prenatal care, most women (30%–75%) self-reported that they did not receive advice from providers on diet, activity, and weight gain.[5] The prevalence of exceeding these guidelines varied by whether the women reported receiving information from a physician. Among women who reported not being given weight guidelines, the prevalence of excessive weight gain was 62.9%; this was significantly higher than among women who reported receiving information from a physician (48%).[5] Moreover, among women who did receive information, these data seemed to indicate an evidence-practice gap between receipt of information and implementation in the women's daily lives.

In addition to the immediate adverse consequences of maternal obesity and/or excess weight gain during pregnancy, growing evidence has suggested that maternal obesity can "program" the baby for disease in future life.[6,7] The most widely investigated programming effect of maternal obesity is offspring obesity. Several observational studies have supported an association between maternal obesity and increased risk of obesity in the offspring as neonates, children, and adolescents. Research has indicated that offspring fat mass and weight circumference in adulthood are also positively related to maternal BMI during pregnancy independent of adult obesity lifestyle factors.[8,9] In addition to studies directly correlating offspring obesity in adulthood with maternal BMI, studies using the surrogate female of offspring birthweight supported a link between maternal obesity and offspring obesity. In linking birthweight and adult obesity, both the Nurses Health Studies (women), N = 163,000,

and the Health Professionals Follow-up study (men), N = 22,000, showed a J-shaped association between birthweight and adult obesity.[10]

Maternal obesity is also associated with several negative pregnancy outcomes, including hypertensive conditions, preeclampsia, gestational diabetes, required induction of labor, cesarean section, having a stillbirth, perinatal death, macrosomia (birth weight > 4000 g), preterm birth (< 37 weeks of gestation), congenital anomaly, increased risk of childhood obesity, and development of type 2 diabetes.[11] Therefore, achieving a healthy weight gain during pregnancy is an important goal for all women.

It is well known that during pregnancy, nutritional requirements are enhanced and women in general respond to this demand by increasing their food intake.[12] Pregnancy represents a unique physiologic state affecting several systems that influence weight, including cardiovascular (increases in cardiac output, heart rate, stroke volume); hematologic (e.g., blood volume); urinary (e.g., renal function); respiratory (e.g., oxygen consumption); gastrointestinal (e.g., constipation, heartburn); and endocrine (e.g., edema, insulin resistance) functions. Psychosocial (e.g., body image, unwanted pregnancies, affronts to self-concept) and environmental (e.g., bed rest) changes also pose unique challenges to maintaining healthy activity levels and eating patterns during pregnancy.[9,10] Moreover, unlike weight control outside of pregnancy, weight control efforts during pregnancy must be carefully regulated to ensure optimal growth and safety for the fetus.[13] However, cultural beliefs, such as "eating for two," may contribute to a caloric intake above the ordinary demands of pregnancy.[14] Since weight gain partially reflects an imbalance between energy intake and energy expenditure, it seems plausible that women during prenatal care visits should be motivated to change their lifestyle towards healthy dietary habits. Additionally, such behavioral changes attained during pregnancy

may persist after childbirth and possibly throughout the woman's life.[14] Therefore, healthcare providers should take advantage of these prenatal care visits as a window of opportunity for implementing effective lifestyle interventions during pregnancy.

Overweight/obesity in women of childbearing age is a serious global public-health concern. In "developing" countries, such as China, from 1992 to 2010, the prevalence of overweight and obesity in women aged 18–44 years increased from 16.8% to 26.4% and from 3.1% to 9.0%, respectively.[15] Of great concern is that these estimates of prevalence are higher in "developed" nations. In the United Kingdom, the prevalence of maternal obesity has more than doubled from 7.6% in 1989 to 15.6% in 2007.[15] For women aged 20–39 years residing in North America, the prevalence of obesity increased from 13.0% in 1993 to 22.0% in 2003.[15] In 2008, data from the Pregnancy Nutrition Surveillance System in the United States showed that the prevalence of pre-pregnancy obesity increased to 28.5%.[15] Since poor birth outcomes, especially high birth weight and low birth weight, have lasting adverse impacts on one's health, education, and socioeconomic outcomes later in life,[16] these research findings have provided support for the promotion of healthy weight among women pre-conception and the prevention of inappropriate weight gain during pregnancy. These factors also implicate significant intergenerational benefits.

Maternal diet during pregnancy represents a specific and modifiable in-utero exposure with the potential to impact developmental pathways that influence future metabolic disease risk.[17] In addition to excess calories, factors within the diet such as fat content and micronutrients may play an important role in fat tissue development and metabolic programming by mechanisms that remain poorly understood. Apart from glucose, little is known in human populations about whether, what, and how specific nutrient exposures impact fetal programming — specifically fetal fat accretion. While fat in the diet is an obvious contributor to the lipid

substrate for adipose tissue growth, the micronutrient components of the diet may play a key role in directly modulating cellular mechanisms that are responsible for adipogenesis.[17] The role of fetal programming in the early development of obesity is an important area of focus for metabolic disease prevention. Unfortunately, there is no current consensus on the most effective content, format, or theoretical framework for gestational weight gain interventions.[18] The literature examining the effect of lifestyle interventions during pregnancy revealed mixed results with major issues related to adherence, efficacy, and feasibility posing as large limitations.[17-23]

One intervention study, the Lifestyle Intervention For Two (LIFT) trial,[22] elicited a more moderate excessive gestational weight gain in a sample of New York City pregnant women. LIFT is one of seven sites in the LIFE-Moms Consortium designed to investigate in pregnant women with overweight or obesity whether various behavioral and lifestyle interventions reduce excessive gestational weight gain and subsequent adverse maternal and neonatal outcomes and obesity in offspring. Each site adopted a different lifestyle intervention protocol, and a description of each can be found elsewhere in the literature.[17] The LIFT intervention focused on diet modification via reduced calorie intake and is based on the DPP and Look AHEAD curricula where the intention was altered from weight loss to control of GWG, as recommended by the 2009 IOM guidelines. The intervention focused on reducing calorie intake and increasing physical activity using behavioral and social support strategies that study counselors delivered in individual sessions. In addition to mitigating excessive gestational weight gain successfully, LIFT had an important and measurable impact on neonatal body composition, providing additional support for the importance of developing interventions that can maintain a healthy material weight gain.[22] However, there were no significant statistical associations with improved diet quality as measured by HEI with either the attenuation in weight gain or the measurable

impact on neonatal body composition.[22] This dissertation aimed to use another measure of diet quality in the context of a paradigm shift in nutrition education, moving the focus from adequate nutrient consumption to quality of whole foods in terms of degree of processing. This dissertation, then, was a secondary analysis of the LIFT data, the aim of which was to explore what, if any, associations exist between maternal diet quality in the context of processing and outcomes of gestational weight gain and neonatal body composition.

Background: Maternal Diet Quality, Gestational Weight Gain, and Neonatal Outcomes

In recent years, growing evidence has supported the notion that the intrauterine environment can "program" or affect pregnancy and neonatal outcomes, as well as subsequent long-term health and development in the offspring; this is referred to as the "fetal programming" or "fetal origins" hypothesis.[24-26] The phenomenon responsible for this fetal origin of diseases is known as developmental plasticity,[7,27] which is an organism's ability to change its phenotype — what an organism looks like as a result of the interactions of its genes (genotype) with environmental circumstances. This plasticity is widely recognized in nature and has a critical period during intrauterine development. Body weight (BW) is frequently used as an indicator of the conditions experienced in utero. The association between BW and subsequent obesity in the fetal origins hypothesis has also been confirmed.[28-30] In this sense, findings from investigating the effects of gestational weight gain on newborn birth weight could have strong policy implications. Recent studies further supported that fetal origins effects can extend to a broader range of lifetime outcomes; specifically, poor health at birth is a key pathway through which deficient or excessive nutrient intake during fetal development exerts persistent effects.[30]

Several structural changes and functional modifications in organs and tissues occur in the fetus to adapt to the surrounding environment as a mechanism of adaptive response that ensures

the viability and survival of the fetus and the newborn.[30] Maternal nutrition during pregnancy is a critical environmental factor, conditioning the development of fetal plasticity and determining the risk of disease in adulthood. Regarding the effects of maternal nutrition, several studies, such as those carried out in a cohort of individuals born during the Dutch famine in the winter of 1944, showed that individuals whose mothers were exposed to famine during pregnancy had a low birth weight and higher risk of obesity, cardiovascular disease, insulin resistance, and hypertension in adulthood.[27-30] Linked to this concept, researchers have developed several hypotheses, such as the thrifty phenotype hypothesis put forward by Hales and Barker.[27] According to their hypothesis, in the presence of exposure to nutrition deficiencies during the in-utero developmental period, there are structural and functional losses of β pancreatic cells as a mechanism that ensures the fetus's viability in order to prioritize the growth of vital organs such as the brain.[27-29] These alterations provide an advantage for survival as long as the nutritional shortage continues. However, when exposure to nutritional deficits ends after birth, moving to adequate or over-nutrient consumption, the permanent adaptations that previously occurred will have negative consequences. Thus, such individuals, during adulthood, would be more likely to develop insulin resistance, type 2 diabetes mellitus,[29-33] and other risk factors associated with metabolic syndrome such as dyslipidemias, hypertension, and obesity.

Studies have demonstrated a BMI-specific association between GWG and neonatal body composition, with higher BMIs being associated with higher neonatal fat mass.[34-38] Excessive fat deposition during early pregnancy could reduce maternal insulin sensitivity and glucose tolerance[34,36] to a greater extent than the normal metabolic processes of pregnancy. This loss of metabolic control could translate into elevated maternal glucose concentration (i.e., glycemic excursions), which exposes the fetus to an increased glucose supply.[33] Both increased supply of

lipid and glucose from the mother may alter the development of fat cells in the fetus, thus resulting in a permanent increase in the fetus's capacity to form new cells in adipose depots in postnatal life.[30] For example, in their study with two independent cohorts of pregnant women, Godfrey et al.[29] found that a low intake of carbohydrates during pregnancy was related to a higher methylation level at the Retinoid X receptor-α (RXRα) promoter region in umbilical cord tissue DNA; the latter was also related to a higher child fat mass index in children at 6 and 9 years of age. At the same time, in terms of quality of carbohydrates, results from glycemic index (GI) dietary intervention studies have shown a higher prevalence of large for gestational age (LGA) births and infants of higher birth weight, higher ponderal index, and higher fat mass born to mothers on the high-GI diet than those on the low-GI diet during pregnancy.[34,36,38] It has been hypothesized that a high-GI diet elevates maternal post-prandial blood glucose concentration, leading to fetal hyperinsulinemia, and possibly higher intrauterine growth rate and increased fetal fat accretion.[34] Moreover, a diet characterized by a high consumption of fried and processed meats — otherwise known as the Western diet — is generally associated with an increased risk of preterm birth, while a diet rich in vegetables and fruits — known as the prudent diet — is associated with a lower incidence of preterm birth.[39] With birth size, prudent diets — such as the health-conscious pattern in the United Kingdom (nonwhite bread, fruits, pasta, and rice); nutrient-dense pattern in the United States (fruits, vegetables, and low-fat dairy); and the rice, fish, and vegetable pattern in Japan—are generally associated with higher birth weight and decreased risks of SGA. Overall, a prudent dietary pattern is generally associated with more optimal birth outcomes. Most studies have been conducted with Caucasians[39] and, to the researcher's knowledge, only one study has investigated the impact of ready-to-eat or ultra-processed food on the maternal diet.[40]

In addition to the research focus of reducing maternal weight before and during pregnancy via reduced quantity of intake, other interventions that could impact fetal overgrowth and offspring adiposity, such as improving maternal diet quality, are warranted. A growing body of literature, mostly secondary analyses, has investigated diet quality and neonatal body composition. Many of these studies used different methods for collecting dietary intake, an already precarious data collection endeavor, and utilized different indices, if any, to measure diet quality.[32-40] For example, Shapiro et al.[35,36] found that poorer diet quality is positively associated with infant adiposity and higher intakes of total fat and saturated fat are characteristics of this poorer diet quality. Shapiro et al. measured diet quality using the Healthy Eating Index (HEI-2010) via a method of 24-hour recall, the ASA-24. Many other secondary analyses stemming from this large trial, and others like it, tend to look at single nutrients. However, Shapiro et al. also suggested that the deleterious effect of these specific nutrients on human neonatal size and body composition may be the result of multiple nutrients interacting.

This highlights the importance of using a measure of diet quality that reflects the whole diet, likely accounting for the synergistic effects of foods and nutrients on neonatal body composition that may not be explained by a single nutrition factor.[36] While there is a growing body of research on fetal fat accretion and neonatal body composition related to maternal diet quality as measured by the HEI and gestational weight gain, little is known about what component(s) of the diet influence fetal fat-free mass accretion. One study, however, did look at the role of macronutrients affecting neonatal body composition.[37] Kizirian found that neonatal fat mass and fat-free mass were significantly associated with carbohydrate and fat intake; the trajectory of the associations was trimester-dependent.

The NOVA Guidelines

Recent dietary guidance, particularly in the U.S., acknowledges the importance of dietary patterns and recommends that people follow a healthy eating pattern across the lifespan with a focus on variety, nutrient density, and limiting calories from added sugars and saturated fats and sodium intake.[41] It also recommends shifting to healthier food and beverage choices. The Healthy Eating Index[42] is based on these recommendations and evaluates people based on the extent to which their diets follow the recommendations. Neither the DG nor the HEI consider the degree of processing related to the foods and drinks recommended, which some researchers have proposed is vitally important.[43-47] They propose that foods can be classified based on degree of processing and not on nutrients and that diet quality can then be judged based on these classifications. This system for classifying foods is called the NOVA system and it has grown in influence over recent years.[48-50]

NOVA proposes that foods can be placed into four food categories based on degree of processing as follows: unprocessed or minimally processed foods (MPFs), processed culinary ingredients, processed foods (PFs), and ultra-processed foods and drinks (UPFD).[47] This food classification approach has been incorporated into international reports on diet and health and has been adopted by national governments for policies on food-based dietary guidelines. In most such reports, the advice has been that (a) MPFs should be encouraged; and (b) the intake of PFs should be moderate; and (c) UPFDs should be avoided. This classification system is shown in schematic form in Figure 1 and in detail in chapter 2.

Figure 1. The NOVA guidelines[47]

Advocates of this classification system are critical of existing food categorizations; they state that they are outdated and their use in nutritional epidemiology focuses unnecessarily on nutrients while ignoring the putative major negative impacts of food processing, as documented in a number of studies.[43-47] As a consequence, the NOVA researchers propose a new paradigm for viewing diet quality because processing alters a number of properties of foods that may have impact on health, apart from its energy or nutrient content. This is shown in Figure 2.

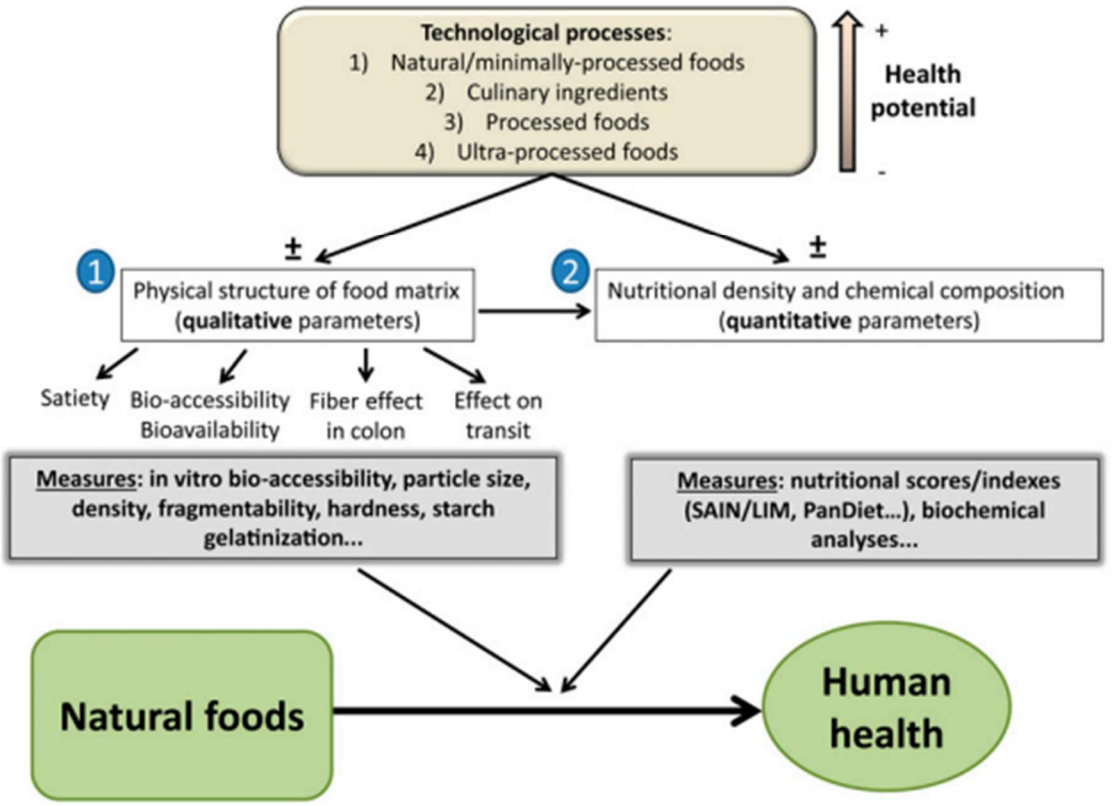

Figure 2. The paradigm shift from reductionist to holistic approach[93]

The present study investigated the impact of degree of food processing on a population of pregnant women with overweight or obesity. There seems to be evidence for this approach Previous research using the NOVA guidelines has been limited and the debate continues about to what degree ultra-processed foods have impacts on human health. This limited evidence has suggested an impact on human metabolic processes, as shown in Figure 2, as well as on overall wellness. In addition, several observational studies have used the NOVA guidelines to determine ultra-processed food intake and investigate associations with various health outcomes. For example, Rauber and colleagues[44] found that ultra-processed food consumption in children significantly predicted increased total cholesterol and low-density lipoprotein as they aged from

6 months to 8 years; for every 1% increase in ultra-processed food consumption, total cholesterol increased by 0.43 mg/dl and low-density lipoprotein increased by 0.369 mg/dl after adjustment for covariates.[44] Another prospective study looked at ultra-processed food consumption and incidence of overweight and obesity in a large sample of adults.[45] The results indicated that participants in the highest quartile of ultra-processed food consumption were at a statistically significant increased risk of becoming overweight or obese. To support this, another group performed a literature review to find that recent research on how ultra-processed foods impact human health demonstrated fairly consistent support for an association between increased rates of obesity and related cardio-metabolic outcomes.[51] Despite this work, there remains a clear need for further studies designed with sufficient control of potential confounders, as is necessary with any new area of research.[51]

Epidemiological studies performed in the United States, Canada, and Brazil have reported increased consumption of ultra-processed foods and utilized similar techniques to apply the NOVA categories to established single-nutrient categories associated with chronic disease.[43-47] For example, Moubarac[44] and Steele[52] used large datasets (FOODEX and NHANES from Canada and the United States, respectively) to investigate the share of ultra-processed foods within the national diet. Not surprisingly, ultra-processed foods contributed to the majority of the dietary share (about 50-60%).[52] In addition, when that share was further analyzed as quintiles, proportions of energy from different macronutrient groups varied, with the highest ultra-processed food consumption also consuming the largest proportions of added sugar and the smallest proportions of fiber within carbohydrate intake; similar results were found for saturated fat intake and salt intake. These studies suggested an association between processed and ultra-processed food consumption and dietary quality, as evidenced by the share of these categories in

public food consumption. However, the sheer frequency of ultra-processed food in the diet alone presents as a confounding factor; more longitudinal studies must be conducted to elucidate further the impact of ultra-processed foods on human health.

There have been some criticisms of the use of the NOVA guidelines. One main argument has focused on the practical difficulty of applying the definition of ultra-processed foods and drinks.

The NOVA classification system proposes the following definition of UPFDs:

> Formulations of several ingredients which, besides salt, sugar, oils and fats, include food substances not used in culinary preparations, in particular, flavors, colors, sweeteners, emulsifiers, and other additives used to imitate sensorial qualities of unprocessed or minimally processed foods and their culinary preparations or to disguise undesirable qualities of the final product.[48]

This definition of ultra-processed food and drink poses a problem in its inherently linguistic parameters; no reference cut-offs for salt, sugar and fat per gram, per portion size, or per unit of energy are designated. Moreover, as for the definition of additives, the user must be able to extrapolate from the presence of an additive to its use in imitating "sensorial qualities of an unprocessed food to disguise undesirable qualities in the final product."[48] This open interpretation can create much confusion when attempting to classify foods from various dietary assessment data. Existing food coding methodologies are largely thorough and clear in how to categorize items, specifically via eliminating any linguistic delineation of categories. In an effort to address these concerns, researchers have developed a carefully defined code system to analyze datasets such as NHANES leaving no ambiguity for how to code foods.[52] In addition, the NOVA guidelines can be applied more objectively once public health nutrition researchers become more familiar with how unprocessed foods change to processed and ultra-processed foods and how this impacts nutrient bioaccessibility.[50]

A second criticism is that the definition of ultra-processed food captures items that are energy dense but not nutrient dense and thus NOVA is capturing energy density and nutrient density. As such, it adds nothing new to existing diet quality measures such as the HEI. To address this criticism, many researchers, and this study, conducted all analyses controlling for calories.

A third criticism is that the NOVA guidelines are unnecessary because there are already existing coding systems for processing of food which are used in government regulations and by food industry to classify its food products in conformity with these regulations.[53] However, it should be noted that these classification systems do not take into account nutritional criteria. Thus, we have a situation where the HEI does not address food source and thus captures only nutrient density with no concern about the state of processing of foods, beyond separating whole fruit and fruit juice, while current systems for classifying foods based on processing do so for regulatory purposes with little consideration of nutrient quality. The NOVA guidelines seek to bridge the two.

A fourth criticism is that the NOVA guidelines are not practical. The categories are not clear so it would be confusing to consumers and thus its usability is in questionn.[53,54] However, the NOVA categories are used as the basis of the dietary guidelines of Brazil and some other south American countries and are being considered elsewhere as well.

Thus, most of the main criticisms of NOVA have been answered. What remains is to continue to investigate the usefulness of the NOVA guidelines for examining the impact of foods on health.

While this study was in progress, one paper was published that investigated the relationships between consumption of ultra-processed foods, gestational weight gain, and

neonatal outcomes in a sample of US pregnant women.[40] The authors concluded that a 1% increase in percentage of intake from ultra-processed foods (PEI-UPF) was associated with a 1.33kg increase in GWG and a 0.22mm increase in thigh skinfold, a 0.14mm increase in subscapular skinfold, and 0.62 percentage points of total body adiposity in the neonate.[40] The authors discussed the usefulness of using the variable PEI-UPF as a predictor of GWG and neonatal total body adiposity. These findings echoed the Healthy Start study conducted by Shapiro, who called for a more comprehensive measure of diet quality in this population.[36]

Results for the primary outcome of the LIFT trial indicated that the intervention group experienced a lower degree of excessive GWG than the usual care group.[22] As a secondary outcome, neonatal body composition was found to differ between the groups with greater fat-free mass/lean mass in the LI group, where neonatal body composition was measured using more advanced techniques than in this recently published study described above.[40] However, the greater neonatal lean mass was not associated with the mitigated GWG. In addition, changes in dietary quality differed between the groups. The lifestyle intervention group had significant improvements in total HEI score, total and whole fruit intake, and decreases in caloric intake from solid fats, alcohol, and added sugar,[22] similar to what Shapiro reported.[36] The change in overall HEI score was not statistically associated with mitigation of maternal excessive gestational weight gain nor with neonatal outcomes. Clearly, there are differences in the way the HEI operationalizes diet quality from the way that NOVA does.

Purpose of the Study

The purpose of this study was to investigate the diet quality of mothers with overweight or obesity and its impact on maternal gestational weight gain and neonatal body composition through the lens of the NOVA guidelines. The investigation was guided by the following questions:

- Does using the lens of NOVA increase a vocabulary to describe diet quality?
- Is there a relationship between excessive gestational weight gain and maternal diet quality as measured by NOVA?
- Is there a relationship between neonatal adiposity and maternal diet quality measured by NOVA?

Specific Aims

Aim 1: Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

1a. Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

Compared to the UC group, mothers in the LI group will have increased percentages of unprocessed food and decreased percentages of ultra-processed foods.

1b. Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

As dietary shares of ultra-processed foods increase, HEI overall scores will decrease.

1c. Compare pre and post ultra-processed food shares of the diet to the pre and post HEI overall scores controlling for calorie intake.

These correlations will weaken when controlling for overall calorie consumption as a covariate.

Aim 2: Investigate the relationship between gestational weight gain and maternal diet quality as measured by NOVA.

2a. Examine whether the independent variable, diet quality as measured by consumption of foods categorized by NOVA as ultra-processed, has an effect on the GWG experience for mothers in both LI and UC related to Post intervention intake of ultra-processed foods adjusted for weight of food and adjusted for total energy intake.

The odds of excessive GWG will be higher for women who had higher UPF intake for both groups.

Aim 3: Investigate the relationship between maternal diet quality as measured by NOVA and neonatal body composition and compare the results of the two anthropometric measures.

3a. Investigate an association between the group differences in maternal diet quality related to ultra-processed food intake as measured by NOVA and neonatal lean mass as measured by QMR.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal lean mass as measured by QMR.

3b. Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal fat-free mass as measured by PEAPOD.

Significance

This is the first study to investigate the association between level of processing as defined by the NOVA categories and maternal and neonatal outcomes using 24-hour recall data and air displacement plethysmography and QMR. In the LIFT study, women in the intervention group experienced a lower degree of excessive GWG, had offspring with significantly higher fat-free mass, and had a significantly higher HEI score than women in the usual care group. If there are associations between maternal diet quality as measured by NOVA and GWG and neonatal adiposity, this may give dietitians, nutrition educators, researchers, and medical practitioners a new vocabulary or direction for structuring nutrition education interventions for this population. To quote Joan Dye Gussow when asked about using butter or margarine, "Perhaps it is time to trust cows more than chemists".[55] Given the global impact of maternal obesity, GWG, and greater childhood adiposity, it seems time to explore the usefulness of processing as a factor in measuring diet quality, so as to be able to elucidate optimal diet qualities to be recommended.

Chapter II

LITERATURE REVIEW

Incidence and Implication of Excessive GWG

Targeting pregnant women has been the focus of dietary and lifestyle interventions, as one third of pregnant women tend to gain excessive weight during their pregnancy.[2,56] Several studies have shown that excessive weight gain during pregnancy is a strong predictor of postpartum weight retention and this may contribute to obesity in women of childbearing age, engaging in a cycle of weight gain.[2] According to the Institute of Medicine (IOM), based on pre-pregnancy body mass index (BMI), normal weight women (BMI: 18.5–24.9) are recommended to gain between 11.4 and 15.9 kg during pregnancy, overweight women (BMI: 25.0–29.9) between 6.8 and 11.4 kg and obese women (BMI: $\geq$ 30) between 5.0 and 9.0 kg.[4] There is evidence suggesting that weight gains within IOM recommendations are potentially associated with healthy fetal and maternal outcomes.[2,5,9,16,57] Although the IOM and other public health and scientific communities have widely disseminated these recommendations, about 55% of women with normal weight and 65% of women with overweight/obesity continue to gain in excess of these guidelines. In standard prenatal care, most women (30%–75%) self-report not having received advice from providers on diet, activity, and weight gain.[6,58] The prevalence of exceeding guidelines among women who had reported not receiving information from a physician was 62.9%; by contrast, the prevalence of exceeding guidelines among women who had reported receiving information from a physician was 48%.[6,58] In addition to the immediate adverse consequences of maternal obesity and/or excess weight gain in pregnancy, growing evidence has suggested that maternal obesity can "program" the baby for disease in future life.[60] The most widely investigated programming effect of maternal obesity is on offspring obesity. There are now several observational studies supporting an association between maternal obesity

and increased risk of obesity in the offspring as neonates, in childhood and in adolescence. It has been shown that offspring fat mass and weight circumference in adulthood are also positively related to maternal BMI during pregnancy independently of adult obesity lifestyle factors. [21,60-63] In addition to these studies directly correlating offspring obesity in adulthood with maternal BMI, further studies using the surrogate of offspring birthweight supported a link between maternal obesity and offspring obesity. Linking birthweight and adult obesity, both the Nurses Health Studies (women) and the Health Professionals Follow-up study (men), large studies of about 163 000 and 22 000 sample size, respectively, showed a J-shaped association (in other words, a positive association at both ends of the curve) between birthweight and adult obesity.[2,63] Maternal obesity is associated with several negative pregnancy outcomes, including hypertensive conditions, preeclampsia, gestational diabetes, required induction of labor, cesarean section, having a stillbirth, perinatal death, macrosomia (birth weight > 4000 g), preterm birth (< 37 weeks of gestation), congenital anomaly, increased risk of childhood obesity, and development of type 2 diabetes.[2,63] Therefore, achieving a healthy weight gain during pregnancy is an important issue for all women.[2]

It is well known that during pregnancy, the nutritional requirement is enhanced and women in general attend this demand by increasing their food intake.[2,10,64,65] Pregnancy represents a unique physiologic state affecting several systems that influence weight, including cardiovascular (increases in cardiac output, heart rate, stroke volume); hematologic (e.g., blood volume); urinary (e.g., renal function); respiratory (oxygen consumption); gastrointestinal (e.g., constipation, heartburn); and endocrine (e.g., edema, insulin resistance) functions.[10] Psychosocial (body image, unwanted pregnancies, affronts to self-concept) and environmental (bed rest) changes also pose unique challenges to maintaining healthy activity levels and eating

patterns during pregnancy.[10] Moreover, unlike weight control outside of pregnancy, weight control efforts during pregnancy must be carefully regulated to ensure optimal growth and safety for the fetus.[63] However, cultural beliefs, such as "eating for two," may contribute to a caloric intake above the ordinary demands of pregnancy.[14] Since weight gain partially reflects an imbalance between energy intake and energy expenditure, it seems plausible that during prenatal care visits, women should be motivated to change their lifestyle towards healthy dietary habits. Additionally, such behavioral changes attained during pregnancy may persist after childbirth and possibly throughout the woman's life.[14] Therefore, healthcare providers should take advantage of these prenatal care visits as a window of opportunity for implementing effective lifestyle interventions during pregnancy.

Overweight/obesity in women of childbearing age is a serious public-health problem, especially in "developing" countries.[15] In China, from 1992 to 2010, the prevalence of overweight or obesity in women aged 18–44 years increased from 16.8% to 26.4%, and from 3.1% to 9.0%, respectively.[14,15] Worryingly, these estimates of prevalence are higher in "developed" nations. In the UK, the prevalence of maternal obesity has more than doubled from 7.6% to 15.6% from 1989 to 2007, respectively.[15] In women aged 20–39 years residing in North America, the prevalence of obesity increased from 13.0% to 22.0% from 1993 to 2003 [15] In 2008, data from the Pregnancy Nutrition Surveillance System of USA showed that the prevalence of pre- pregnancy obesity increased to 28.5%.[15] Since poor birth outcomes, especially high birth weight and low birth weight, have lasting adverse impacts on one's health, education, and socioeconomic outcomes later in life, the findings of this research suggested promoting healthy weight among women before pregnancy and preventing inappropriate weight gain during pregnancy can generate significant intergenerational benefits. In the literature, there

is a glaring lack of SES, family, and environmental level data. This review attempts to describe the knowledge of the scientific community surrounding factors of gestational weight gain and its impact on neonatal adiposity with a focus on fetal programming via diet quality. This review also examines intervention studies related to attenuating gestational weight gain and what conclusions can be drawn to inform further research, practice and policy.

An Area of Nutrition Intervention Literature With Many Gaps

The consistent and robust data supporting the independent effects of maternal diet during pregnancy (broadly measured) and maternal BMI on fetal growth and size provide clues to potential pathways and mechanisms that need to be further explored. The Shapiro study suggested that poor overall diet quality, as assessed by the HEI-2010, during pregnancy may lead to increased neonatal adiposity, regardless of maternal BMI. This highlights the potential importance of dietary interventions during pregnancy, likely a more accessible time for clinicians and public health practitioners to communicate the importance of healthy eating to pregnant women. Evidence-based strategies for optimal implementation are not currently clear.[8-10,17-23,56–58,63-67] The role of maternal diet in influencing these variables remain poorly understood, which limits the ability for clinicians and public health officials to educate pregnant women on appropriate consumption in pregnancy to improve maternal and neonatal outcomes.[68] Lifestyle intervention studies have implemented a number of different strategies to achieve attenuation of gestational weight gain. This review looks at this attenuation in relation to overnutrition and neonatal adiposity as possibly indicative of intrauterine programming of obesity. In addition, this review will highlight the strengths and limitations of this type of research and how the literature can inform research and practice.

Table 1. A Summary of GWG Intervention Studies

Author	Year	Location/ Setting	Participants	Sample Size	Intervention	Outcome Measures	Conclusion	Strengths/Limitations
Herring	2016	Urban Pennsylvania from outpatient clinic	Low Income, AA OW/OB from outpatient clinic	UC = 29; LI = 27; N = 66	Women recruited from OB clinic; treating staff blinded, RCT of 12-week tech-based intervention focused on EI, PA and SMP	Proportion of women with excessive GWG; neonatal size outcomes and intervention engagement	p = .0333 for primary measure; no other differences; tech is very effective; weight loss adjunct to practice also more effective	Pilot study, larger N needed, one of two studies focused on this population, tech-based approach, theory-based
Tussey	2016	Rural Mississippi in home	Low income, mostly AA, 2nd trimester	UC = 33; LI = 26; N = 59	Monthly home visits of parent trainers (PAT) and derived from DPP/Infant and focus on healthy eating and GWG per IOM	Proportion of women with excessive GWG; neonatal size outcomes and intervention engagement	Not effective	AA women administered protocol; only monthly visits, small n, perhaps intervention topics too broad, possibility of conflict with other HCPs, geographically hard to avoid UPFs
Phelan	2018	Urban California/ outpatient	OW/OB <16 wk. preg, Hispanic	UC = 127; LI = 129; N = 256	Face-to-face visits every two weeks; partial meal replacement focused on controlling excessive GWG, PA, SM	Weekly GWG, HEI, questionnaires, blood biomarkers, intervention engagement	Intervention successful for controlling rate and excessive GWG (p = .02; .0001; .03) behavior played a big role, particularly dietary restraint. Reduction in TGs, with negative trends for other biomarkers,	First to really look at Hispanic, albeit ASA24 not validated for population. Measures not collected mid-pregnancy to bolster rate of GWG perspective

Table 1 (continued)

Author	Year	Location/ Setting	Participants	Sample Size	Intervention	Outcome Measures	Conclusion	Strengths/Limitations
Dodd	2015	Australia Public metro hospital	OW/OB women	LI = 488; UC = 482 (subset of 215/179 for BIA)	Diet, PA, Behavioral every 2 weeks	Skinfold thickness and body circumferences, weight and length, some BIA	No statistical significance between groups	Robust methodology albeit not the most accurate; great inter-observer reliability. No pre-pregnancy BMI or control for GWG in model
Grivell	2016	Australia Public metro hospital	OW/OB women	LI = 935; UC = 912	Diet, PA, Behavioral every 2 weeks	Ultrasound measures of fetal growth and fetal adiposity, mid-thigh, abdominal wall	Thigh and abdominal differences between groups	Robust methodology albeit not the most accurate; great inter-observer reliability. No pre-pregnancy BMI or control for GWG in model
Gallagher	2017	OW/OB women-NYC	White, higher SES	LI = 105; UC = 105	Diet, PA, Behavioral every 2 weeks	PEAPOD, qMR, HEI, Accelerometer data	Higher lean mass in LI neonates, not associated with GWG; although intervention was efficacious with a very significant difference between groups ($p < .03$)	Advanced technology, robust approach to intervention design

One of the gaps in the literature that this review identified is a consensus on optimal and efficacious education and intervention for prenatal and antenatal nutrition to meet the IOM guidelines that are applicable for many across the socioeconomic spectrum.[5,56,66] The following studies have shown that dietary education can significantly reduce gestational weight gain among pregnant women and in some trials among overweight and obese women as well. Herring et al.[56] investigated the effects of a novel intervention approach for a population of pregnant African American women living in the United States with overweight or obesity. The 12-week technology-based approach of text message reminders and encouragement, along with phone consults to deliver education focused on energy intake, physical activity, and reinforcement of self-monitoring behaviors, allowed for underserved women to have access to treatment not offered in their clinic setting. Phelan et al.[57] conducted an intervention with pregnant Hispanic and non-Hispanic populations with overweight or obesity; this intervention included in-person nutrition education also focused on energy intake, physical activity promotion, and self-monitoring behaviors. In addition to lifestyle education, this protocol also included partial meal replacements, where the intervention group was asked to replace two meals with the provided meal replacement. Both of these studies resulted in statistically significant effects on the primary outcome of controlling GWG and on the secondary outcome of intervention engagement and adherence. It is worth noting that both of these studies included interventions that were rooted in behavior change theory. The Phelan study also saw a statistically significant difference of lower triglyceride levels in the intervention group; this may be a result of the lower calorie intake in this group.[57] Albeit not significant, one limitation of this study was that HEI scores collected via the ASA-24 were only measured once and could have been markedly different earlier in the intervention. Lastly in this cluster, a study looking at pregnant African American women with

overweight and obesity of low socioeconomic status living in the lower Mississippi Delta region was unable to detect a significant difference between the control and treatment groups with regard to proportion of women with excessive GWG and neonatal outcomes.[66] This intervention, although evidence-based, was not rooted in behavior change theory and was focused on education only as the program was developed from the DPP and integrated into a Parent as Teachers program. Participants received monthly home visits from study staff of similar background. However, many environmental challenges were faced in this particular setting. These included too broad a scope of the intervention, conflicting perspectives with other health care providers, a small sample size, infrequent visits, and the ubiquitous access of ultra-processed foods. In addition, retention rates were lower in this study than in the previous studies mentioned in this section; this population was also reported to be younger than the populations studied in Phelan, but similar to the population studied in Herring. One conclusion that could be drawn here to influence research and practice is to further investigate the role of technology-based intervention and possibly incorporate more social support through various social media platforms, as Smartphone use is overwhelmingly frequent in young populations and mobile Health (mHealth) is constantly being developed.

A handful of intervention studies has looked at not only gestational weight gain, but also neonatal adiposity as an outcome as well. Different methodologies related to collection of anthropometrics have yielded different results, even within the same study population. As a secondary outcome of the LIMIT trial, adiposity was measured by two different methodologies.[64,65] The first paper published neonatal adiposity based on the results of skinfold assessment and bioelectrical impedance.[64] The second paper published fetal adiposity results based on ultrasound technology.[65] The LIMIT intervention included the three major tenets of

energy intake control, increased incidental physical activity, and self-monitoring behaviors, all delivered by study dietitians and other trained study staff in person or via phone every 2 weeks until 36 weeks of gestation. In addition, there was a significant improvement in HEI scores and select HEI categories (related to increased whole food intake) for the intervention group; these were statistically significantly different from the control group. The studies measuring neonatal and fetal adiposity had conflicting results; the sonography methodology was able to detect differences in fetal adiposity between intervention and control groups, where the neonatal skinfold methodology did not find any statistically significant difference between the groups. Both studies used robust methodology; however, the advances in technology may have been able to detect a difference that skinfold could not ascertain, even in the presence of a statistically significant reduced relative risk of infants with birthweight > 4kg.[65] However, it is important to note that the ultrasound technique used in the Grivell study, albeit advanced, comes with many limitations and should be interpreted with caution. More recently, Gallagher et al.[22] published neonatal adipose results from a lifestyle intervention (LIFT) derived from the DPP and Look AHEAD trials, administered by the study dietitian every 2 weeks. Participants were also asked to self-monitor food intake in between counseling sessions. The intervention was able to elicit a statistically significant difference in diet quality as determined by the overall HEI score and specific categories between the two groups (again related to increased whole food intake and decreased SOFAAS scores); in addition, the primary outcome of neonatal adiposity was also significantly different between the two groups. Methodology consisted of using QMR and air placement plethysmography (PEAPOD). Neonates born to the intervention mothers had significantly higher amounts of lean mass and similar fat mass as neonates born to the mothers in the usual care group. Potential mediators of this increase in lean muscle mass may be related to

diet quality; there was no statistical significance between amount of GWG and neonatal adiposity.[22]

Future research is needed to understand how to increase involvement of practitioners in counseling of diet, physical activity, and weight control. Innovative methods are needed to increase provider time and insurance coverage for lifestyle counseling so that the burden does not fall on community outreach for those affected by lower socioeconomic status. Also, studies are needed for testing the effects of greater practitioner training or patient assertiveness training in broaching topics related to diet, physical activity, and weight control. Moreover, science-based public health recommendations for prenatal diet, physical activity, and weight control may change between pregnancies. Women with prior pregnancies should be encouraged to seek up-to-date information about prenatal recommendations. While much more research is required, it appears that consistent lifestyle education and behavior change intervention rooted in evidence and theory that meet participants where they are at are optimal for affecting quality of life for offspring. Clinicians should focus on the tenets of self-monitoring behaviors and incorporate other healthcare professionals to assist in administering the lifestyle counseling.

A recent review by Nelson et al.[59] looked further into the modifiable determinants of maternal metabolism and obesity, along with describing the impact that maternal obesity, rate of gestational weight gains, and modifiable determinants of the diet has on primary fat accretion of the fetus, occurring during week 13 and 35 of gestation, as demonstrated in previous studies. In addition to diet, other modifiable determinants include physical activity along with specific interventions for various socioeconomic status. However, this extensive literature review concluded that the population of pregnant women with overweight or obesity requires much

attention from the research community in an effort to help attenuate the maternal obesity epidemic.[59]

Fetal Programming

In recent years, evidence has accumulated and supported the notion that the intrauterine environment can "program" or affect pregnancy and neonatal outcomes, as well as subsequent long-term health and development in the offspring; this is referred to as the "fetal programming" or "fetal origins" hypothesis.[69] The phenomenon responsible for this fetal origin of diseases is known as developmental plasticity,[7,27] which is the ability of an organism to change its phenotype in response to environmental circumstances. This plasticity is widely recognized in nature and has a critical period during intrauterine development.[31] BW is frequently used as an indicator of the conditions experienced in utero. The link between environmental stressors and later disease has become a discipline of medicine, now called the development origins of chronic disease.[26,27,70] The association between BW and subsequent obesity has also been confirmed in several studies.[28-32] In this sense, findings from investigating the effects of gestational weight gain on newborn birth weight will have strong intervention and possibly food policy implications. Recent studies have further shown the "fetal origins" effects can extend to a broader range of lifetime outcomes and, in particular, poor health at birth is a key pathway through which deficient or excessive nutrient intake during fetal development exerts persistent effects.[30]

Structural changes and functional modifications in organs and tissues occur in the fetus to adapt to the surrounding environment transferred by the mother, as a mechanism of adaptive response that ensures the viability and survival of the fetus and the newborn.[7-31,71-74] Maternal nutrition during pregnancy is a critical environmental factor, conditioning the development of

fetal plasticity and determining the risk of disease in adulthood.[31] Regarding the effects of maternal nutrition, several studies, such as those carried out in a cohort of those born during the Dutch famine in the winter of 1944, pointed out that individuals whose mothers were exposed to famine during pregnancy had a low birth weight and higher risk of obesity, CVD, IR, and hypertension in adulthood.[27] Linked to this concept, several hypotheses have been developed such as the thrifty phenotype hypothesis, put forward by Hales and Barker.[27] In this hypothesis, they suggested that in the frame of deficient nutrition conditions during pregnancy, there is a structural and functional loss of β pancreatic cells as a mechanism that ensures the viability of the fetus, giving priority to the growth of vital organs such as the brain. These alterations provide an advantage for survival as long as the nutritional shortage continues. However, if this situation ends after childbirth, moving to a good or over-nutrient consumption, the permanent adaptations that have previously occurred will have negative consequences. Thus, such individuals, during adulthood, would be more likely to develop IR and T2DM[29,30] and also other risk factors associated with MS such as dyslipidemias, hypertension, and obesity.

Excessive fat deposition during early pregnancy could reduce maternal insulin sensitivity and glucose tolerance[32] to a greater extent than the normal metabolic sequelae of pregnancy. This loss of metabolic control could translate into elevated maternal glucose concentration (i.e., glycemic excursions) which exposes the fetus to an increased glucose supply.[32] Both increased transfusion of lipid and increased supply of glucose from the mother may alter the development of fat cells in fetus, thus resulting in a permanent increase in the fetus's capacity to form new cells in adipose depots in postnatal life.[32,60]

In a landmark paper published in 2003, Dr. Patrick Catalano further investigated the Pedersen hypothesis by comparing neonatal anthropometry from mothers with normal glucose

tolerance to mothers with GDM.[69] The Pedersen hypothesis states that fetal overgrowth or macrosomia is a consequence of increased maternal glucose, which stimulates fetal insulin production and possible other growth factors.[69] This paper also emphasized the review by Sparks, which hypothesized that genetic factors have a stronger relationship with neonatal fat-free mass, whereas in utero environment may correlate better with fetal fat mass. In addition, this paper noted that there has been a 33% increase in the incidence of T2DM over the last decade, particularly in young adults with obesity.[69] This compounds the issue of GWG; we are seeing more obesity throughout our population, especially in our younger members. This paper tested the hypothesis that women with GDM will have neonates with increased fat mass and not FFM, compared to infants of women with NGT due to the relationship between GDM, T2DM, obesity, and the Pedersen hypothesis.[69] Neonatal body composition was evaluated via TOBEC. The infants of the women with GDM have significantly greater ponderal indexes and skinfold measures at all five sites, compared with the NGT group. Although there was no significant difference in the proportion of infants with weight >4000g between groups, there were significantly more infants whose weights were >90th percentile for gestational age in the GDM group, compared with the NGT group ($p = .004$). The infants of women with GDM had significantly greater body fat and percentage of body fat in comparison with the NGT group. Additionally, the distribution of fat was not significant in the circumferences of the abdominal/thigh and chest/thigh ratios between the groups. However, the significant differences in percentage of body fat remained such even after adjustments. TOBEC estimates of body composition showed that infants of the women with GDM had significantly less FFM. Splitting the GDM group into women who were treated with diet alone versus treated with diet plus insulin and skinfold measures were significantly greater in the A2 group compared with NGT.

TOBEC estimates of fat mass and percentage of body fat were also significantly greater for A2 infants compared to the A1 infants. Maternal height was a significant variable with respect to birth weight and FFM and will be important to be considered as a covariate in further investigations into neonatal FFM.[69,70]

Maternal Diet Quality

It remains unclear which maternal fuels and metabolic measures have the most substantial impact on fetal growth, body composition, and fat accretion and at which stage of pregnancy.[70-75] Mothers who have a high BMI may impart a detrimental proinflammatory environment for the fetus that leads to an increased risk for chronic disease.[76-79] Grandy et al.[70] in 2017 performed a secondary analysis of a prospective observational pilot study on the effect of third trimester maternal body composition and diet in pregnancy on placental function and fetal growth. Women were of varying pre-pregnancy BMIs; diet quality was collected via 24 hour recalls and assessed using the HEI. Neonatal measurements were taken via skinfolds. Here, the focus was using a nutrient density model and logistic regression was used to assess the relationship between HEI score and adherence to GWG recommendations, along with ANOVAs to look at diet quality and neonatal adiposity. However, this group found no significant differences or associations between diet quality, GWG, and neonatal adiposity in the third trimester.[70] Higher HEI scores were inversely associated with infant birth weight and length. This finding suggested that as a women's diet quality decreases, the likelihood of having a larger infant as measured by weight and length at birth increases.[70] Clinical guidelines and recommendations for nutrient intake during pregnancy assume that maternal weight added during this time is affected by diet, generally focusing on recommending healthy eating and exercise to gain within the recommended amount.[77,78,80,81] In contrast, these findings suggested

that third trimester maternal diet quality is unrelated to GWG.[70] Conversely, poorer diet quality rather than caloric intake may be related to higher infant birthweight and length at birth.[72]

In contrast to the Grandy study is the Crume study,[77] one of the secondary analyses to come out of the Heathy Start study led by Allison Shapiro.[35,36,73] Crume noted that a progressive elevation of circulating maternal lipids was observed in later gestation as a normal physiological response to optimize availability of substrates for fetal growth and development.[77] In this larger cohort of 804 mother-infant pairs, Crume set out to evaluate associations between circulating levels of glucose and lipids at <24 weeks' pregnancy and at >32-weeks' gestation and neonatal body composition. Air displacement plethysmography (ADP) was used to measure neonatal body composition outcomes. Diet quality was assessed via the ASA24. The majority of the cohort had a healthy pre-pregnancy BMI. Investigators found that increasing maternal fasting glucose levels and HOMA-IR in both early and late pregnancy were linearly and positively associated with neonatal FM and FM%, independent of maternal age, parity, race/ethnicity, diet, physical activity, and gestational weight gain. A significant interaction was detected between total cholesterol levels in the second half or pregnancy and maternal pre-pregnant BMI on the relationship of neonatal outcomes.[77] Glucose levels in the second half of pregnancy were strongly associated with neonatal adiposity after controlling for the large confounder of pre-pregnancy BMI. In contrast, HOMA-IR had a strong influence on FM and FM%, independent of pre-pregnancy BMI. These results suggested time-dependent specific intrauterine effects of maternal insulin resistance and glucose levels during pregnancy on fetal and neonatal fat accretion.

Nevertheless, solid studies of diet composition and related fetal outcomes remain sparse and conflicting. A better understanding of the role that diet quality and composition play in

determining GWG and its sequelae could lead to new modifiable risk factors appropriate for targeted interventions.[81]

Godfrey et al.[29] carried out a study in two independent cohorts of pregnant women and found that a low intake of carbohydrates during pregnancy was related to a higher methylation level at the Retinoid X receptor-α (RXRα) promoter region in umbilical cord tissue DNA, and the latter was also related to higher child fat mass index in children at 6 and 9 years. RXRα hypermethylation is associated with a decrease of its expression and with obesity development in rats.[30] White rice has a high glycemic index (GI) and is known to be a major contributor to dietary glycemic load in Asia.[39,82] This finding was reminiscent of results from GI dietary intervention studies that have shown a higher prevalence of LGA births and infants of higher birth weight, higher ponderal index, and higher fat mass born to mothers on the high-GI diet than those on the low-GI diet during pregnancy.[33–37] It has been hypothesized that a high-GI diet elevates maternal post-prandial blood glucose concentration, leading to fetal hyperinsulinemia, and possibly higher intrauterine growth rate and increased fetal fat accretion.[33-36,76-81]

Whereas diets characterized by a high consumption of fried and processed meats, otherwise known as the Western diet, are generally associated with an increased risk of preterm birth, diets rich in vegetables and fruits, known as the prudent diet, are associated with a lower incidence of preterm birth.[82] With birth size, prudent diets such as the health-conscious pattern in the United Kingdom (nonwhite bread, fruits, pasta, and rice); nutrient-dense pattern in the United States (fruits, vegetables, and low-fat dairy); and the rice, fish, and vegetable pattern in Japan are generally associated with higher birth weight and decreased risks of SGA. Overall, it seems that a prudent dietary pattern is generally associated with more optimal birth.[82]

Table 2. A Summary of Studies Looking at Impact of Maternal Diet Quality on Neonatal Adiposity

Author	Year	Location/Setting	Participants	Sample Size	Maternal Measures	Neonatal Measures	Conclusion
Horan	2015	Secondary analysis of ROLO study (IRE)	Secundigravid women with previous macrosomic baby	N = 542 mother-infant pairs	Low GI or UC; questionnaire and food diaries, maternal anthropometry	Neonatal anthropometry	BW negatively associated with 3rd trimester vitamin d intake, positively associated with B12.
Horan	2014	Secondary analysis of ROLO study (IRE)	Secundigravid women with previous macrosomic baby	N = 542 mother-infant pairs	Low GI or UC; questionnaire and food diaries, maternal anthropometry, OGT	Neonatal anthropometry	Diet evaluated using DASH parameters; neonatal central adiposity associated with smoking, pre-pregnancy BMI, upper arm circumference,

Table 2 (continued)

Author	Year	Location/Setting	Participants	Sample Size	Maternal Measures	Neonatal Measures	Conclusion
Shapiro	2017	Colorado prenatal obstetrics clinic (USA); Healthy Start prospective cohort	Pregnant women >16 yo with <24 weeks gestation	N = 173 mother-infant pairs	ASA24, FFQ, usual intake via "NCI method" UCT for SIRT1, avg daily niacin intake	Neonatal ADP/skinfolds,	Maternal high fat diet was a significant and independent predictor of %FM and FM
Moore	2017	Colorado prenatal obstetrics clinic (USA); Healthy Start prospective cohort	Pregnant women >16 yo with <24 weeks gestation	N = 1078	ASA24, FFQ, DII scores, CRP and IL-6	Neonatal ADP/skinfolds,	Among women who were obese pre-pregnancy, a proinflammatory diet associated with increased neonatal adiposity; higher DII score increased odds of LGA baby

Table 2 (continued)

Author	Year	Location/Setting	Participants	Sample Size	Maternal Measures	Neonatal Measures	Conclusion
Shapiro	2016	Colorado prenatal obstetrics clinic (USA); Healthy Start prospective cohort	Pregnant women >16 yo with <24 weeks gestation	N = 1,366	ASA24, FFQ, HEI	Neonatal ADP/skinfolds	HEI scores <57 significantly associated with higher FM but not different FFM reflecting an increase in FM not a loss of FFM
McKenzie	2017	Maternity wards (AUS)	Singleton deliveries with GA >34 weeks and ADP within 24 hours	N = 142	FFQ à CHO intake g/d CV and categorical quartiles	ADP	No association of carbohydrate quality/quantity intake with birth weight or fatness
Kizirian	2016	Secondary analysis of the GI Baby 3 study (AUS)	Singleton with GDM risk at weeks 14-20	N = 96 for mid, 88 for end	Low GI: High fiber; food records	ADP	Mid-pregnancy, only carbohydrate, total fat and saturated fat were significant. carbohydrate energy was negatively associated with FFMI; late pregnancy higher carbohydrate associated with lower FMI, high proportions of carbohydrate from high GI sources predicted lower FFMI; trimester specific effect with quantity and quality
Brei	2018	Secondary analysis (GER)	32yo White normal pre-preg BMI	186 for 15th week pairs and 167 for 32nd week pairs	2 7-day diet records with portion size counseling	MRI, child anthropometry not neonatal	15th week – fiber negatively associated with central adiposity in children; week 35 total fat associated negatively with body comp

outcomes. Most existing studies have been conducted in Caucasians [82] and few studies have looked at the impact of ready to eat or ultra-processed food on the maternal diet.[40,83-85] Bayol et al.[24,83] determined perirenal fat mass in rats exposed to a "junk food" or a "normal" diet, all on the background of either maternal junk food intake during pregnancy or normal diet during pregnancy. Not surprisingly, rats exposed to a junk-food diet both post-weaning and in utero had the greatest perirenal fat mass, and one that was substantially greater than rats never exposed to junk food. Rats exposed to junk food post-weaning, but not in utero, also displayed greater perirenal fat mass compared to normal-diet controls, albeit less pronounced than those exposed to junk food in utero. Of perhaps most surprise, however, rats exposed to junk food in utero, but then transferred to chow diet postnatally, also showed increased perirenal fat mass compared to controls (these differences reaching statistical significance in males but not females), indicating that the in-utero effects of maternal obesity have consequences long beyond pregnancy.

A shift in research focus from reducing maternal weight before and during pregnancy to other interventions that could also impact fetal overgrowth and offspring adiposity, such as improving maternal diet and nutrition, is warranted.[35] Findings from a study by Shapiro et al.[35,36] that poorer diet quality is positively associated with infant adiposity and higher intakes of total fat and saturated fat are characteristics of this poorer diet quality suggested that the deleterious effect of these specific nutrients on human neonatal size and body composition may be the result of multiple nutrients interacting. This highlights the importance of using a measure of diet quality that reflects the whole diet, likely accounting for the synergistic effects of foods and nutrients on neonatal body composition that may not be explained by a single nutrition factor.[36]

Shifting From Nutrients to a Wider Lens

The obesity pandemic has coincided with the mass production and proliferation of cheap, energy-dense nutrient poor foods and beverages, and robust epidemiological studies have shown that diets are the primary driver for unhealthy weight gain[43-46,51,88-91] Contextually, it has been argued that transnational corporations are major drivers of populations switching from whole or minimally processed foods to high-processed foods and beverages.[85] Reversing community appetite for highly processed, artificially flavored foods/beverages that are aggressively marketed will be challenging, given the ubiquity and hyper-palatability of these products.[92]

Many in the nutrition research community are in consensus that processed/ultra-processed food has contributed to the rising prevalence of obesity and chronic disease and that perhaps we are moving away from a paradigm where we discuss nutrition over nutrients.[47,93] In a 2011 commentary, Dr. David Ludwig [88] discussed three major revolutions in technology with the advancements related to the introduction of fire, agriculture, and, most recently, industry. The Industrial Revolution of the 19th century allowed for mass production of refined flour and concentrated sugar, setting the stage for what might be termed the commodity-based diet,[43] characterized by food extrusion technology, petrochemicals, and biotechnology. Currently, products terms as ultra-processed, a term coined by Monteiro et al.,[48] are widely disseminated and may even resemble natural foods, but actually represent a radically new creation. Many of these foods contain highly processed ingredients never before present in the food supply.

A diet based on ultra-processed products may promote obesity and chronic disease through a variety of mechanisms, including higher energy density, large portion size, low content of fiber, micronutrients and phytochemicals, poor quality dietary fat, high glycemic load, and high-intensity flavoring promoting increased intake. Swinburn et al.[89] defined drivers of the

obesity epidemic as an environmental factor that has changed substantially during the past 40 years, is global in nature, and is rapidly transmissible. Obvious possible drivers stem from the food system: increased supply of cheap, palatable, energy dense foods; improved distribution systems to make food much more accessible and convenient; and more persuasive food marketing.

Carlos Monteiro discussed this at length with regard to the assessment of what is ultra-processed; Monteiro and colleagues developed and introduced the NOVA guidelines in 2010.[48] The literature related to these guidelines is growing at a rapid pace and is somewhat controversial as it does address the ubiquitous presence of the "commodity-based diet" via large transnational food companies.[91,92] After covering what the NOVA guidelines are and how they were developed, this review describes the presence of ultra-processed foods in the global diet, in addition to illustrating the logistical use of the NOVA guidelines in research and some of the major criticisms surrounding the use of NOVA and the context of the criticisms. In addition, another focus of this review describes the impact of these food products as characterized by the NOVA guidelines on human health and highlights the gaps in the research that the secondary analysis attempts to fill.

In the paper first introducing NOVA,[48] Monteiro wrote how many organizations have taken quite a cavalier approach to food-processing classification, with critics adjusting taxonomy guidelines to how they suit them.[91] When taking an approach of categorizing foods according to their botanical or animal origins, foods with very different nutrient profiles and impacts on eating and health such as whole grains, breakfast cereals, flours, breads, cookies, crackers, and cereal-based snacks such as power bars are classified within the same food group of grains or cereals and cereal products. The same applies to whole fresh fruits, sugar-canned fruits, and

reconstituted fruit beverages, all classified as fruits. These classifications of the big four or five are derived from old and moot classifications that are not representative of our current food supply.[91,92] The NOVA guidelines have been criticized for being too stringent on what constitutes across the levels of processing, but it is important to note that subsequent observational studies have been more squarely focused on ultra-processed food intake, with no provision of limitations surrounding the other three categories.[47-49]

Originally divided into three categories, a fourth category acknowledging not only the distinction of what the health implications are to have a food be ultra-processed, but also the vast plethora of foods that fall into a category that is consistently associated with nutrients to limit thematically group together as different than simply "processed."[48] Fardet and colleagues published a review related to the impact of food processing classification systems in 2015.[47] The paper discussed that given our current global nutrition climate, it seems more relevant to capture diet quality that classifies foods based on their level of processing, rather than their botanical or animal origins.[47] Fardet and colleagues supported this statement by reiterating that our environment provides us with a large range of transformed/processed foods and epidemiology studies have consistently shown that prudent, health, vegetarian, Nordic, and Mediterranean-style dietary patterns are more protective than the Western diet.[47] Fardet discussed a new paradigm that proposed that food heath potential should be first defined by both its food structure and nutrient density and that the impact of processing on these factors should be more extensively and systematically measured.[47] He provided examples of foods that are the same, but due to their differences in processing, do carry different health effects.[47,50] One example was increased consumption of pickled vegetables which can cause atrophic gastritis; another is the difference of brown rice, which has a protective effect against type 2 diabetes, and white rice, which increases

type 2 diabetes risk when consumed in high amounts. He also highlighted areas of interest in the literature when researchers have inadvertently looked at processing in the past. For exanple, a large body of reseach has looked at raw versus processed fruits and vegetables, full fat versus low-fat dairy items, whole versus refined grains, and red and processed meats.[47] The outcomes of these studies have been able to determine themes where certain items, apparently due to some characteristics of the processing, have measureable impacts on disease states while the same food processed differently elicits another health response.[47] Fardet highlighted the importance of describing different types of food processing, their health implications, and devising methods to measure per food how it should be treated in terms of nutrition guidance.

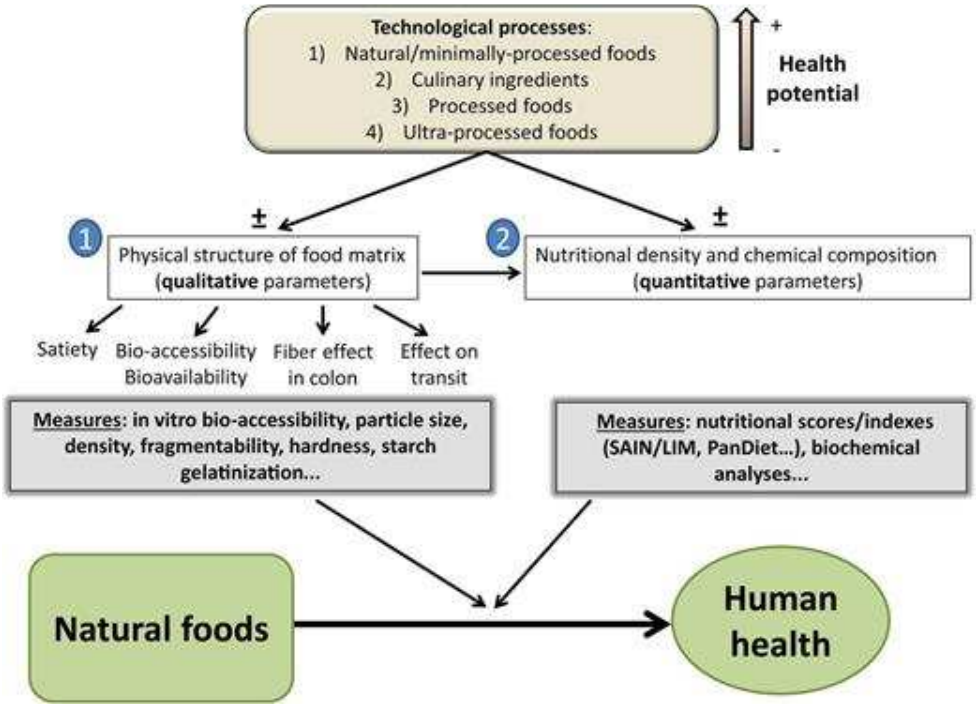

Figure 3. Fardet's (2015) model

Moubarac (2014) [50] performed a systematic review to evaluate the quality of current methods to assess diet quality via food processing. Here, Moubarac stated that what he and his team found in the literature of nutritional epidemiology appeared fragmented. His team used a well-constructed criterion to determine the quality of the studies' assessment of food processing

within diet quality.[50] These were five criteria which included that the processing assessment be specific, coherent, clear, comprehensive, and workable. From a term search yielding 1,276 papers, only 21 were able to be evaluated as having used a classification system.[50] From this, five food processing classification systems were identified: the International Agency for Research on Cancer's European Prospective Investigation in Cancer and Nutrition (IARC-EPIC) from Europe; the International Food Information Council (IFIC) from the US; the National Institute of Public Health (NIPH) from Mexico; the International Food Policy and Research Center (IFPRI) from Guatemala; and lastly, NOVA, which was deemed as being global. From these five, the reviewers rated NOVA as being of the highest quality according to its criteria.[50.] The rationale for this included that NOVA was the only system derived from a formal definition of food processing; it was completely specific, coherent, and comprehensive. It was mostly clear because the classification used in early publications had some aspects which now have been updated, adjusted, and clarified. It is rated as mostly workable, and at the time was pending further studies. The NOVA system was followed by the NIPH system from Mexico being rated as only partially specific, being that the distinction between industrial and local foods is in terms of the form and scale with which they are marketed rather than their properties and nature. The third highest-ranking classification system was the IARC-EPIC system from Europe, as it did not fully distinguish between cooking and industrial processing and lacked a set of classification criteria.[50] Finally, the US and Guatemalan systems ranked lowest; Moubarac stated that these systems were incomplete and unclear in various ways and would need development to be applied to different contexts or to surveys using different methods of dietary recall.[50] It is important to note that authors of this paper were also members of the research team responsible for developing NOVA. However, as the health implications of ultra-processed food increasingly

mount,[43-46,51,93- 97] it is necessary to have a clear system that allows identification of food processing that is benign and food processing that is malignant. Another recent review from Michelle Crino et al.[98] also explored similar frameworks. While not comparing classification systems using the same criteria as Moubarac and including two other frameworks not mentioned in the previous review, the discussion noted the fact that NOVA was actually the most technical and, therefore, had great disagreement when assigning foods into categories. The research team employed somewhat limited efforts to determine agreement and disagreement between classification systems for a single food; this was somewhat curious as they were not all using the same definitions of processing, and here is where consensus is needed.

Monteiro's paper published in 2013 [91] examined trends in the purchase and sales of a specific type of processed food product in high- and middle-income countries with special attention to Canada and Brazil. Determinants of these trends and their impact on the quality of diets and on health, along with policy implications, are also discussed.[91] The author had no intent to deny a need for food processing for the progress of man, but the nature, extent, and purpose of food processing have been revolutionized as an intrinsic part of industrialization.[91] He reiterated the steady declines in food insecurity and nutrient deficiencies and how ultra-processed foods may have surpassed their goals in effectively ensuring that all are fed.[91] He highlighted the cheap fatty sugary foods followed by rapid increases in chronic non-communicable diseases since the 1980s and directly related it to the increased invention of palatable products from cheap ingredients and additives, transnational food and drink manufacturing, distribution, retailing, fast food, and allied enterprises whose profits derive from ready-to-eat products.[91]

Monteiro defined ultra-processed foods as ready to consume, entirely or mostly made from industrial ingredients, and being extremely profitable.[48,49,91,92] The ultra-processed foods

are made from processed substances extracted or refined from whole foods—oils, hydrogenated oils, fats, flours/starches, variants of sugar, and cheap parts or remnants of animal food with little or no whole foods. Examples include burgers, frozen pasta, pizza and pasta dishes, nuggets and sticks, crisps, biscuits, confectionery, cereal bars, carbonated and other sugary drinks, and various snack products. Most are made, advertised, and sold by large or transnational corporations and are very durable. Typically, ultra-processed foods are energy-dense; have a high glycemic load; are low in dietary fiber, micronutrients, and phytochemicals; and are high in unhealthy types of dietary fats, free sugars, and sodium.

Monteiro's (2013) paper also noted the social and economic shaping of our food industry that is of transnational origin: Big Food, Big Soda, Big Snack, as he referred to it, are on level with the gross national product of middle-size countries, and that by implementing so much processing into our food supply, we are inherently "teaching the world to snack."[48,49,91,92] Previous and more detailed analyses showed ultra-processed foods have displaced and are displacing staple foods such as potatoes in Canada and rice and beans in Brazil, displacing other foods such as legumes, milk, and fruits in Canada; milk, cassava, and fruits and vegetables in Brazil; and culinary ingredients in both countries.[43,46,99,100] This displacement transforms food supplies and, thus, food culture and dietary patterns. The most striking change in the food systems of high-income countries, and now of low- and middle-income countries, is displacement of dietary patterns based on meals and dishes prepared from unprocessed or minimally processed food by those that are increasingly based on ultra-processed food and drink products.[92] The result is diets with excessive energy density, high in free sugars and unhealthy fats and salts, and low in dietary fiber that increases the risk of obesity and other diet-related non-communicable diseases.[43,46] The proportion of ultra-processed products in food supplies can

be seen as a measure of overall population diet quality. By the early 2000s, ultra-processed foods had risen to over half of all calories consumed in Canada, and to over one quarter in Brazil.[92] Limitations included in this paper were related to data analysis—not all types of ultra-processed products listed in data were included. This was due to aggregation of products that prevented precise identification.[92]

At the time of this literature review, the NOVA guidelines have been used in Chile, Norway, Brazil, United States, United Kingdom, Australia, Mexico, New Zealand, Spain, Canada, and many other countries to explore relationships between non-communicable diseases (NCDs) such as cardiovascular disease (CVD), obesity and metabolic syndrome.[43-46,51,93- 97] Researchers have been interested in exploring the impact on intakes of nutrients to limit and descriptions of shares of diet as described by NOVA.[43-46,51,94-97,101,102] NOVA studies have demonstrated that per head sales of sweet/savory snacks increased by 50% in upper middle-income countries and 100–300% in lower middle-income countries.[91] Studies based on NOVA have shown that the consumption of ultra-processed food increases overall energy density and content of saturated fat, trans fat, and free sugars, while decreasing fiber, phytoestrogens, magnesium, vitamin K, vitamin A, iron, and zinc, among other key micronutrients.[46,96] While many critics of NOVA are quick to argue this by saying that ultra-processed foods tend to be fortified and provide the population with nutrients they may otherwise become deficient in,[53,54] ultra-processed foods are not simply modified foods with additional vitamins, but they are formulations of industrial sources of dietary energy and nutrients, particularly unhealthy types of fats, starches, free sugars, and salt plus additives, including those designed to intensify sensory impact.[91] As a research community, these additives in particular have simply not been around long enough for us to determine the long-term safety of intake. They typically contain little or

even no intact food yet continue to increase in consumption. Ultra-processed products expressed as a percentage of total purchased calories in this study have increased continuously; in Canada, ultra-processed food consumption sat round 24.2% of total calories in 1938; this increased to 54.9% in 2001.[43,96] Brazil has a similar trajectory with 18.7% in 1987 to 26.1% in 2003.[43,96]

Eicher-Miller [103] was the first investigator to describe the contributions of processed food to dietary intake in the United States, specifically focused on NHANES dietary intake data collected between 2003–2008. Published in 2012, she clearly stated that recommendations for a healthy diet based on the level of food processing did not yet exist at the time of her writing, but referred to a recent classification for food based on processing level completed by the International Food Information Council.[103] Eicher-Miller defined food processing as any deliberate change made in a food from the time of origin to the time of consumption.[103] This was a much broader and all-encompassing definition, including cooking, canning, fortification, and packaging. This broad definition seemed to lend itself to a criticism of the NOVA guidelines as being much too stringent in their recommendation of avoiding processed foods. The IFIC categories of food processing included minimally processed, foods processed for preservation, mixtures of combined ingredients, ready-to-eat processed foods, and prepared foods/meals with increasing intensity of processing.[103] However, in the data analysis, it was discovered that not all foods could be captured within these categories, as insufficient information was available to determine categories for food originating in restaurants, schools, dining halls, or other eating establishments into one of the categories.[103] From using these particular categories, the investigators found that food processing can add nutrients to the diet to help meet the DRIs via enrichment and fortification.[103] The investigators then stated that nutritional deficiency and inadequacy were prevented as a result of processed food intake,[103]

despite the literature demonstrating the high accessibility to, palatability of, and predisposition to selecting ultra-processed food.[93,97,104] However, the investigators also presented concerns regarding the processing of food contributing to intake of "food components to reduce" such as sodium, added sugars, and solid fats; there seemed to be a suggestion that the effects of these nutrients can be offset by adding other nutrients or other favorable components such as fiber. This study provided evidence for both the benefit and concerns regarding processed foods.[103] This group concluded that generalized public health messaged based on such a ranking would be simplistic or misleading and that processing level is not a major determinant of foods' nutrient contributions to the diet nor does it have a clear association with health.[103]

Three studies analyzing the contribution of ultra-processed foods to the US dietary intake via NHANES data used the NOVA guidelines and found something different from the previous Eicher-Miller study. Steele (2016, 2017) [52,101,102] all demonstrated that ultra-processed foods as classified by the NOVA guidelines tended to contribute to a majority of Americans' intakes of "food components to reduce." In Steele (2016),[101] the investigators looked at the contribution of ultra-processed foods to added sugars in the US diet. Organizations such as WHO, AHA, Canadian Heart and Stroke Foundation, USDGAC, and UK National Health System have all come to a consensus that a high intake of added sugars increases the risk of weight gain, excess body weight, obesity, type 2 diabetes, hypertension, stroke, coronary heart disease, cancer, and dental issues.[101] In addition, foods higher in added sugars are often higher in empty calories with minimal essential nutrients fiber and displace more nutrient dense foods. Added sugars are defined as sugars that are added to foods as an ingredient during preparation, processing, or at the table.[101] According to the US Dietary Guidelines for Americans (DGA), the diet should be composed of no more than 10% added sugars — this is a challenge if we are not addressing

ultra-processed foods in the diet. This study specifically used the What We Eat in America dietary component using two 24-hour recalls, with one in person and one over the phone, for a total of 9,317 matched recalls. N = 280,132 food codes from FNDDS, which were classified according to NOVA, in a similar fashion as the Eicher-Miller study had done with the IFIC categories. The investigators found that UPF contributed to almost 60% of calories and 90% of added sugars in the American diet.[101,102]

Steele [102] and Louzada [96] looked at the consumption of ultra-processed foods and their findings reported that it was directly linked to the energy density of diet and content of saturated fat, trans fat, and free sugar, and inversely associated with fiber and protein.[51,96,102] It is well established that micronutrient deficiencies are among the 20 most important risk factors for diseases and affect around 2 billion people worldwide. For this study, data were used from the Brazilian Household Budget Survey between 2008–2009.[102] Again, data were analyzed from two 24-hour recalls with 1,120 food items listed in this database. Micronutrients evaluated were A, B12, C, D, E, niacin, pyridoxine, riboflavin, thiamine; minerals were calcium, copper, iron, phosphorous, magnesium, manganese, selenium, and zinc expressed as mg or mcg/1000kcal. Individuals were classified into five strata in accordance with their consumption of ultra-processed foods; quintiles of population distribution were according to contribution of UPF to total caloric value of the diet; mean daily EI 1866 kcal/day with 69.5% category 1, 9% category 3, and 21.5% category 4. Ultra-processed foods contained significantly less (not even half) of amount of essential vitamin and minerals (14/17 compounds above).[102]

Many other studies have drawn a harder line, demonstrating observational and cross-sectional evidence from many populations on the impact of the increased intake of ultra-processed foods on the world's health. The cardiovascular risk related to Metabolic syndrome

(MetS) appears to persist from childhood into young adulthood and there also appears to be an increased prevalence of MetS with overweight and obesity.[46] The Tavares study, published in 2011, was a cross-sectional study based on CAMELIA data (Cardio-metabolic-renal) conducted between 2006–2007.[46] This study included adults with hypertension and/or diabetes mellitus and controls and their living biological children aged 12–30 years assisted by the Family Doctor Program in Brazil.[46] The analysis included children 12–19 years coming from 185 families (n = 210).[46] Data collected included covariates such as age, race, educational level, household income per capita, smoking, PA, and screen time collected via questionnaire (PA, last 15d time and type).[46] Weight, height, waist circumference, BMI, blood pressure, high-density lipoprotein, glucose, and triglycerides were also collected after a 12-hour fast.[46]

Dietary intake was assessed via semi-quantitative FFQ 90 food items with 17 questions related to eating habits.[46] These intakes were then transformed into daily frequencies and converted into grams or milliliters. The investigators used official US food composition tables to estimate intake related to macronutrients. This study classified foods into three NOVA categories (the original iteration of the NOVA). Diagnosis of MetS was based on cutoff of hyperglycemia. The researchers controlled for familial confounders using generalizing estimating equations (GEE), which produced efficient estimates for regression parameters with correlated data. Data for energy intake were categorized into quartiles. Higher consumption and lower consumption were compared to verify association with MetS. Prevalence Ratios (PRs) were estimated by Poisson regression.[46] Investigators found 66.2% normal weight with 31.4% OW.[46]

Table 3. Comparison of IFIC and NOVA Food Processing Classification Systems

IFIC	NOVA
Minimally Processed: washed and packaged fruits and vegetables; bagged salads; roasted and ground nuts and coffee beans	Category 1: removal of inedible or unwanted parts, drying, crushing, grinding, fractioning, filtering, roasting, boiling, pasteurizing, NA fermentation, refrigeration, chilling, freezing, placing in containers, or vacuum packing
Food Processed for Preservation: canned tuna, beans and tomatoes; frozen fruits and vegetables; pureed and jarred baby foods	Category 2: pressing, refining, grinding, milling, drying
Mixtures of Combined Ingredients: some packaged foods, such as instant potato mix, rice, cake mix, jarred tomato sauce, spice mixes, dressings and sauces, and gelatin	Category 3: various preservation or cooking methods, with most category 3 foods have 2-3 ingredients, with the purpose of processing to be increased durability or sensory qualities
Ready-to-Eat Foods: breakfast cereal, flavored oatmeal, crackers, jams and jellies, nut butters, ice cream, yogurt, garlic bread, granola bars, cookies, fruit chews, rotisserie chicken, luncheon meats, honey-baked ham, cheese spreads, fruit drinks, and carbonated beverages	Category 4: not modified foods but formulations made mostly from substances derived from foods and additives, including casein, lactose, whey and gluten, further processing of category 2 such as hydrogenated or interesterified oils, hydrolysed proteins, soy protein isolate, maltodextrin, HFCS, invert sugar. Additives include: dyes, colors, color stabilizers, flavors, flavor enhancers, non-sugar sweeteners, and processing aids such as carbonating, firming, bulking, anti-bulking, de-foaming, anti-caking, glazing agents, emulsifiers, sequestrants and humectants.
Prepared Foods/Meals: Prepared deli foods and frozen meals, entrees, potpies and pizzas	---

Most common disturbances were reduced high-density lipoprotein, increased serum glucose, increased waist circumference, abnormal blood pressure, and increase triacylglycerols. There were no significant differences between boys and girls. MetS was diagnosed in 6.7% of participants mostly in overweight adolescents.[46] Adolescents with MetS had a higher average daily energy and macronutrient intakes, and intake from Category 3 foods was higher compared with those who had no component ($p = .035$) and one/two components ($p = 0.012$).[46] There were no differences between average consumption of category 1 and 2 foods between adolescents with and without MetS. The regression models were significant for MetS, ultra-processed food and smoking, as well as with increased carbohydrate intake, increased energy consumption, and family history increase of triacylglycerols.[46] There were no associations between presence of MetS and sociodemographics and behaviors except smoking and no association between protein or fiber.[46] Energy intake remained a significant variable across models 1 and 2 (smoking and family history), but carbohydrate intake was only significant once adjusted for family history.[46] Ultra-processed food intake remained significant across all three models.[46] Intake of simple carbohydrates discussed was speculated upon a possible rationale for presence of MetS components.[46] Diets were high in flour, pizza, hamburgers, snacks, and sweets associated with abdominal obesity, changes in blood lipids, and glucose.[46] This population also had a high intake of sugar-sweetened beverages. Limitations included the cross-sectional design, FFQ, family history of CVD, and lower cutoffs for MetS. The study concluded an association between MetS with some aspects of dietary intake.[46]

Moubarac (2012) [43] introduced the important issue of increasing weight and rapid rise of chronic disease and its possible relationship to increased production and consumption of readily available ultra-processed foods. This team echoed Monteiro by saying that the fact that the foods

which are causing all this human strife are either elided or understated and noted that food classifications were created at a time when obesity was a non-issue and rarely addressed in dietary intake assessment. At the time of this paper's publication in 2012, NOVA was still three categories and only Brazilian studies had been conducted. The data analyzed came from FOODEX (Food Expenditure Survey) 2001. A questionnaire was collected on data related to income and other socioeconomic variables. Data on food purchases were collected over 14 days from one person in each household covering 98% of Canada.[43] Meals and snacks bought in restaurants only had information on expenditure and were not included in the analysis.[43] Interviewers visited households at the end of the recording phase to make sure all diaries were complete.[43] Any missing information was extrapolated from other nearby households re: amounts and costs. Purchased food quantities were used as the units of analysis and converted into units of energy; food codes in FOODEX were matched with food codes from CNF (Canadian Nutrient File).[43] Food purchases were assigned to one of the three NOVA categories. Some compromises had to be made as CNF did not distinguish between unsweetened and sweetened fruit juices and so on.[43] Mean estimates and SEs for relative contribution of each food group and food item to the total household energy availability were calculated for the whole population.[43] Calculated conventional nutritional indicators were for the average Canadian household food basket and also for two simulated baskets, one containing only category 3 items and the other basket category 1 and category 2; items were kept in the same ratios as the national food basket, i.e., for category 3 basket, if bread and confectionary showed up at 10% and 5%, then appeared as 2:1 in simulation.[43] Results were then compared for WHO indicators of chronic disease: protein, fat, saturated fat, carbohydrate, free sugar, fiber, and sodium.[43] These were averaged out for low levels of PA and investigators used a correction factor to account for

cooking or preparation losses.[43] Investigators then calculated the same nutritional indicators to quintiles of the distribution of the relative contribution of Category 3 products to total energy availability and compared using linear regression. All models were adjusted for household income. The mean per capita energy availability of 2,129 kcal/day; 25.6% from category 1, 12.7% category 2, and 61.7% category 3.[43]

From the results of this paper, Canada appeared to have more ultra-processed food consumption than the Tavares paper was concerned with MetS; investigators postulated this may be related to cooking and food preparation methods in high-income to high middle-income countries.[43] Data showed that a Canadian diet high in ultra-processed food exceeded WHO upper limits for fat, free sugars, and sodium, in addition to falling short of fiber recommendations.[43] The lowest quintile of ultra-processed food intake coming still exceeded energy density recommendations. The investigator suggested changes to saturated fat content to help with this excess of energy intake. The main finding was that 80% of the Canadian population had diets that included more than 50% of ultra-processed foods in terms of energy.[43] It was not possible to manipulate these diets to make them correspond with WHO and other recommendations designed to prevent and control obesity and related chronic disease. One could conclude that cooking was the answer, with saturated fat being much more easily identifiable in home cooking than in prepackaged ultra-processed food. The limitations of this study included that not all food purchased represents food consumed; it did not include restaurant purchases and the unit was households, not individuals, which may have skewed results. The author supported the recommendation to use FFQs/24-hour recalls when assessing diet quality via NOVA and concluded that a healthy diet for Canada would include less than one third of energy from ultra-processed food.[43]

Juul (2014) [94] reported that ultra-processed foods currently made up 75% of the world's food sales. This includes sugary sweetened beverages (SSBs), trans fat, and processed meats, which have been conclusively linked to poor health outcomes but not enough intervention on all ultra-processed foods or the glaring factor that all these wildly different foods that are ultra-processed foods were left out. The aim of this study was to investigate the consumption of ultra-processed foods in Sweden from 1960 on and to see whether such changes were reflected in national obesity statistics.[94] Data were pooled from several sources. Data concerning direct food consumption came from the Swedish Board of Agriculture based on total quantity of food that reached private households, restaurants, and catering establishments, including those of public facilities such as schools and hospitals. Amounts consumed directly by producers were also included. These were classified according to the food's original nature and each group was further subdivided into group. The Swedish National Food Agency calculated per capita intake based on estimated consumption. There were no data on bean/legumes, and fresh fish and seafood were not reported between 2000–2010 as estimates were considered unreliable by the Board of Agriculture with no reason reported. Household food spending was also collected. Four thousand randomly selected households were selected, and three interviews and records of all expenses for 14 days were conducted. BMI data backed only to 1969. Data were classified according to category 1, 2, 3-1, and 3-2 (ultra-processed). Issues with classification arose similar to other papers, as some items that UPF were grouped into unprocessed (i.e., juices, nuts). Trends in energy and macronutrient consumption were also investigated. SSB accounted for 40% of the increase in UPF alone. Sweet and savory snack foods increased by 367%. Increases in fat and protein and decreases in carbohydrate were also seen. Obesity and overweight increased. Minimally processed food consumption remained relatively unchanged, but mean increase in

energy intake along with anthropometrics also increased. The investigators also discussed increased eating rate along with marketing and availability as being determinants for increased consumption of ultra-processed foods.[94]

Rauber (2014) [44] looked at elevated lipids tracked from childhood into adulthood and if processed and ultra-processed food consumption at preschool age predicted increases in blood lipid levels. Five hundred mother-child pairs were recruited with face-to-face interviews conducted at 6 months, 3–4 years, and 7–8 years postpartum. Phone calls were made to 10% of the population at monthly intervals. At 3–4 and 7–8 years, two 24-hour recalls were collected on two non-consecutive days chosen randomly within 2 weeks to 1 month. Mothers provided data on 3–4, self-reported on 7–8. Blood samples were collected at each time point. Ultra-processed food intake was significantly associated with increases in low-density lipoproteins and total cholesterol. The authors concluded that unless overconsumption of ultra-processed foods was curtailed, other interventions focusing on fruit and vegetable consumption would have limited impact.[44]

In addition, another study in France looked at consumption of ultra-processed foods and cancer risk.[95] Using logistic regression, the researchers were able to predict incidence of cancer diagnosis using ultra-processed food intake as the independent variable. With a large sample size of n = 104, 980 participants, mostly female, found that those with the highest intakes of ultra-processed foods tended to be younger, current smokers, and less educated with less family history of cancer and lower physical activity level.[95] Conversely, they had higher intakes of energy, lipids, carbohydrates, and sodium, along with lower alcohol intake. From the total contribution of ultra-processed food in the diet (18.74% for men and 18.71% for women), main food groups contributing to the ultra-processed share of the diet were sugary products (26%),

drinks (20%), followed by starchy foods and breakfast cereals (16%), and ultra-processed fruits and vegetables (15%).[95] The main finding of this study was that ultra-processed fats and sauces ($p = .002$) and sugar products ($p = .03$) and drinks ($p = .005$) were associated with an increased risk of overall cancer and ultra-processed sugary products were associated with risk of breast cancer ($p = .006$).[95] Overall, in this large prospective cohort, a 10% increase in ultra-processed food consumption was associated with significant increases of 12% in the risk of overall cancer and 11% in the risk of breast cancer.[95] While the limitation of being unable to limit all potential confounders certainly existed in this study and the population was primarily female, it is possible that the strengths of the significant findings were actually being underestimated due to the lack of generalizability with a mostly female sample.[95]

A study similar to the one proposed within these chapters by Rohatgi et al.[40] also looked at the population of pregnant women and their ultra-processed food intake with a focus on the outcomes of gestational weight gain and neonatal adiposity. Dietary data were collected from food frequency questionnaires administered to a fairly diverse population ($n = 45$) who were of either lean or obese status between weeks 33 and 35 of gestation. This cohort continued to gain another 12 kg on average between week 33 and delivery (around week 40). Using similar process as proposed within these chapters of assigning foods into NOVA categories, the investigators found that higher intakes of ultra-processed food expressed as a percentage of energy intake significantly predicted higher rates of gestational weight gain for the mother ($p = .016$) and increased skinfold thickness at subscapularis ($p = .045$) and thigh ($p = .026$) and body fat percentage ($p = .037$) as measured by skinfolds in the neonate. In addition, these investigators also found that only PEI-UPF was a significant predictor for body fat percentage of the neonate ($p = .035$) from a model including HEI 2010 scores, total calories, and total fat intake. Although

the FFQ may have posed as a limitation, it is important to note that this includes a different time point than from a 24-hour recall; this assumed intake from the month preceding.[40]

A recent review by Poti (2017) [51] acknowledged marked changed in the global diet, with ultra-processed foods displacing whole or minimally processed foods. It also acknowledged NOVA as most specific, coherent, comprehensive framework for the assessment of food processing within a diet. The aim of the review was to summarize and critique the evidence evaluating the association between ultra-processed food intake and obesity as a limited number of studies had looked at ultra-processed foods and health. The review also included food consumption as well as food purchases. There were an N = 10; 3 on ultra-processed food and obesity, 3 for all age groups, 3 on pediatrics, 4 adults.[51] Most studies were from Brazil, one in UK, 2 from Spain, 1 from Canada, 1 from Guatemala. A variety of dietary intake data collection methodologies were employed. The majority of studies were cross-sectional, while only three employed a more rigorous longitudinal study and no RCT exist at the time of publication. Some of the discussion included an absence of mechanistic links to obesity, independence from nutrient content and a universal lack of accepted definition of ultra-processed food. Mendonca [45] study had the strongest evidence as a longitudinal study; there is a critical need for future studies with similar designs to confirm in different populations, locations, and contexts. Five studies investigated cardiometabolic outcomes. Poti highlighted the need for refined dietary assessment methods: FFQ being a primary issue and suggested that studies need to be repeated with 24-hour recall data similar to NHANES.[51] In addition, studies need to adjust for physical activity, smoking, alcohol, and other potential confounders.

Literature regarding the quasi-addictive nature of foods is also growing rapidly. Some ultra-processed foods can give an impression of being healthy with reduced sodium, artificial

sweeteners, and the like.[93] Intense palatability, in addition to omnipresent and aggressive sophisticated marketing, equals unlikely modest consumption; thereby, ultra-processed foods may also harm endogenous satiety mechanisms and promote energy overconsumption and, thus, obesity. To further discuss the implication of the quasi-addictive nature of ultra-processed foods, Fardet et al. conducted a study published in 2016 [93] that was the first study to look at food structure and implications on satiety signals. Data from the satiety index (SI), the glycemic glucose equivalent (GGE), the glycemic index (GI), and the NOVA guidelines were correlated. The results of this study showed strong correlations between GGE, SI, and degree of food processing, whereas the GI did not correlate with degree of processing. The more a food is processed, the higher the GGE and the lower the SI. In addition to this result, another finding was that the measurement of GGE was more linked to processing than GI required replication. These findings were important in terms of implication of dietetic practice.[93]

Comparison With Dietary Quality Indices (HEI/AHEI/DASH/aMED)

Food *patterns* can be defined as the quantities, proportions, variety, or combination of different foods and drinks in *diets,* and the frequency with which they are habitually consumed. For the duration of nutrition research here in the United States, the majority of the literature has focused on single nutrients rather than categorizing food intake in patterns of consumption. For example, a healthy diet pattern may consist of fruits and vegetables and whole grains, whereas another individual may have a dietary intake consisting of a majority of sweet snacks and desserts. Diet quality indices such as the Healthy Eating Index are increasingly being used in epidemiological research form which we derive dietary recommendations.[105-109] However, the methods for measuring diet quality and analyzing its relationship with the risk of death varies across studies and this has hampered the formulation of dietary recommendations.

The concept of healthy eating patterns has been adopted by the Dietary Guidelines for Americans over time, as a growing body of research has emerged on the health benefits of eating from specified food groups. The Dietary Patterns Methods Project (DPMP) [109] has the explicit goal of conducting standardized and parallel analyses on the prospective association of select dietary patterns as characterized by dietary quality indices and mortality outcomes in three large cohort studies in the United States, including the NIH-AARP Diet and Health Study (AARP study), the Multiethnic Cohort (MEC), and the Women's Health Initiative Observational Study (WHI-OS). DPMP investigators considered a broad range of dietary indices and selected four with particular relevance for dietary guidance that had been commonly used in US populations: the Healthy Eating Index 2010 (HEI-2010), the Alternative Healthy Eating Index (AHEI 2010), the alternate Mediterranean Diets (aMED) score, and the Dietary Approaches to Stop Hypertension (DASH) score. Aims of the DPMP included looking at correlations between these dietary patterns within and across cohorts; if higher diet quality as measured by these indices is consistently associated with lower cardiovascular disease and cancer mortality risk; and where the threshold for benefit begins and how diet quality as measured by these indices relates to absolute intake amounts of food groups, foods, beverages, and nutrients across the cohorts. The DPMP findings showed moderate to strong Spearman's correlation coefficients between pairs of index scores observed in all cohorts. Correlations between HEI and DASH were the highest, with the lowest correlations observed between HEI and aMED. In addition, all four indices were able to show reduced risk of aforementioned mortalities comparing quintile 1 (lower) to quintile 5 (higher scores). However, it must be noted that these are FFQ data; meal preparation and food source have no space on these particular dietary intake assessments. Also, there are many

similarities between the four indices with regard to their recommendations, but some differences remain, whereas not one is all encompassing of salt, trans fat, and whole foods.[109]

Recently Tseng et al. in 2018 [104] published a paper that aimed to evaluate the effect of replacing less processed foods with ultra-processed foods in a diet designed to meet the DGA. The approach was to compare the nutrient content of two menus: one USDA sample menu and a comparable UPF version. The primary finding was that substituting UPF in a sample menu developed to meet DGA guidelines resulted in a menu that provided fewer calories but more sugar and sodium. Mean daily energy content was 274 calories less on the ultra-processed diet than the less processed diet. While providing more sugar and 500mg more sodium than the recommended upper limit, the ultra-processed products were not of those that were considered by the participants to be cheap, unhealthy, or extremely processed. This statistically significant difference in nutrients to limit between diets of medium and heavy reliance on ultra-processed foods is also meaningful in a public health context. In addition, the ultra-processed menu here was 20% more costly than the original menu.[104]

A recent study by Lavigne-Robichard [110] was published explicitly using the NOVA guidelines alongside other indices. A group associated with Moubarac from Canada looked at diet quality indices in relation to metabolic syndrome in an Indigenous Cree population. In this study, logistic regression was also used to describe relationships between diet quality scores and MetS. The measurements used were the alternative Healthy Eating Index (aHEI), the Food Quality Score (FQS), and NOVA. This was the first study to report information on diet quality and food processing related to MetS among Indigenous peoples, notably the Eeyouch adults. Diet quality scores were low and ultra-processed food intake relatively high at 52%. Their results showed that NOVA scores of ultra-processed food intake were a better predictor of MetS than

aHEI or FQS in this population. The aHEI may not have been generalizable to a population such as Indigenous peoples and, interesting to note, the FQS has no reliance on nutrient intake. It is also important to note that the dietary assessment tool used to gather the data may not be the most efficacious tool to use with an Indigenous population.[110]

However, there are critics of the NOVA guidelines, especially surrounding application to various populations.[53,54] Gibney (2017) [54] published a critical appraisal of the approach of focusing on processing as a metric of diet quality versus as individual nutrients. Gibney felt that the guidelines, with their heavy linguistic definition, posed a problem for defining foods and pointed to the HEI as being able to recognize and categorize foods; there was no need to envelope processing into measures of diet quality. He felt that the guidelines were open to many interpretations, and with no cutoffs for salt, sugar, and fat per gram, per portion size, or per unit of energy, and not dependent upon the presence of additives, too subjective to be applied to large datasets. He also postulated that educators and consumers would need to know more about additives, i.e., which additives mimic sensorial qualities and which disguise undesirable qualities. He argued that the foods listed in the categories do not match the normal standards typical of food classification and would not be able to work with Foodex, EPIC, LanguaL, SR codes, FNDDS Food codes, and so on. Moreover, Gibney stated that no arguments have been offered for how or if food processing constitutes a consumer health risk through adverse nutrient intake or chemical or microbiological hazards. However, one concrete example is trans-fat in ultra-processed foods and this predates the concept of UPF by decades. Monteiro countered that "the significance of industrial processing—and in particular methods and ingredients developed or created by modern food science and technology—on the nature of food and on the state of human health, is so far understated."[100]

Application of NOVA is not without substantial research challenges and contradictory findings. Gibney stated that the NOVA classification system is of no value because it cannot offer specificity at the individual nutrient level and thus does not offer more than HEI or AHEI. Gibney argued that significant changes in diet quality were not impactful enough on the public health scale. Like other critics, Gibney also posed the question regarding vitamin and mineral insufficiency with decreased ultra-processed food intake. To address the claims from the Fardet camp regarding satiety and processing,[93] Gibney pointed to the fact that the ultra-processed food and eating addiction literature is sparse and inconclusive.

Monteiro responded to this criticism by highlighting Gibney misinterpretation of the category 4 foods; Gibney communicated that it is based on macronutrients and not the nature, purpose, and extent of food processing.[100] NOVA has been used to quantify shares of ultra-processed food in the diet for not only added sugars and micronutrient displacement, but also trans-fat, increased energy intake, and so on.[52,96,101,102] Gibney's claim that added sugars are part of the definition is also false according to Monteiro.[100] Monteiro addressed that all food is processed in some way and that Gibney's writing directs reader to leave the paper, thinking anything outside of unprocessed is considered food to avoid from the NOVA group standpoint. Gibney failed to cite the Medonca studies, illustrating a dose response over time to the observed relationship between increased BMI and ultra-processed food intake. To counter Gibney's point about the poor workability of the NOVA guidelines in the context of data analysis, Monteiro refuted the idea that the system is crude and pointed to several studies to date linking NOVA's ability to predict nutritional quality of diets and disease risk.

Jones (2018) [53] also published a criticism of the NOVA guidelines. She made similar mistakes to Gibney regarding NOVA interpretation. Jones attempted to compare the NOVA

definition with legal, technical, popular press, and public health definitions, albeit the initial inaccuracy of her interpretation of the guidelines. She made a direct comparison to IFIC and seemed to find the categories of NOVA too broad. Specifically, the issue presented in her paper was focused on the designation of foods with more than five ingredients or the presence of added sugars or additives as ultra-processed. She then concludes that any association of ultra-processed food with obesity or metabolic syndrome and the like would be based on tautological logic as this definition arbiters via presence of additional calories. Her paper seemed to highlight the congruence of the already established definitions of processed foods while downplaying the differences in the details. This surely presented as an issue in the Eicher-Miller analysis, specifically related to the IFIC categories of processing.[53,103]

Eicher Miller [103] discussed that use of the IFIC (International Food Information Council) guidelines will result in all foods in the diet may be assigned to one of the IFIC Foundation categories on the bases of complexity of processing and the physical chemical and sensory changes found in food as a result of processing.[103] Thus, foods contained within an IFIC Foundation category may undergo different specific processing techniques but maintain a similar state of change compared with their original unprocessed state.[103] Eicher Miller's study did not seem as streamlined in terms of interpreting the categories. Some examples of this included deli meats. Rather than classified as prepared foods/meals, they were assigned to a new category, "ready to eat processed foods."[103] Ready to serve, canned, condensed soups would be categorized as "mixtures of combined ingredients." Finally, insufficient information was available to classify foods from restaurants, schools, and dining halls, and thus another category was created, "foods from restaurants or dining halls."[103]

Jones stated that the goals of processing are to increase shelf life, maintain or enhance food safety and nutrient quality, address specific nutritional requirements, and add variety and convenience. She discussed consumer confusion and this might be the role that dietitians can play in food label education. Tseng [104] addressed consumer confusion and highlighted another potential role for registered dietitians and other health care professionals. She referred to this as "flawed substitutive behavior," which is the replacement of perceived unhealthy foods with foods that are often higher in energy, fat, sugar, and sodium. Educating consumers about ultra-processed foods is a potential strategy to reduce confusion. Another recent publication from Weaver [111] concurred with this, describing data from NHANES 2003-2006 that clearly demonstrate that inadequacy would ensue if people were to altogether stop eating processed or ultra-processed food. However, the IFIC and the NOVA guidelines would certainly categorize cereals differently; Froot Loops and Bob's Red Mill oat bran would be placed in similar categories for IFIC but different categories for NOVA. From this analysis, it seems that Vitamins A and D, folate, and iron would decrease in the population's intake.[111] However, from Eicher Miller's paper and issues with categorizing foods using IFIC, we see incredible consistency across the age groups studied, namely >2 years, 2-18 years, and >19 years in relationship to highly-processed food intake. Minimally processed foods accounted for only ~300 kcals/day; processed foods provide ~1,200 kcal/day and majority of sodium, added sugars, dietary fiber, iron and folate, and saturated fat along with considerable amounts of D, calcium, potassium, and B-12.[103] Foods from dining out provided ~600 kcal/d and a considerable amount of some nutrients to the American diet (>20%).

Jones stated that food scientists are most judicial in that foods are categorized on a continuum based on the complexity of the processes, not the number or kinds of ingredients.[53]

She also added that additives, salt, and sugars are regarded as part of the recipe and can help fulfill the goal of processing which, of course, is not to make cheap food for the masses regardless of health impact, but is also helpful for consumers and farmers to reduce pre- and post-harvest losses, to minimize resource use, decrease waste, maintain safety and quality, and offer convenience. Jones stated that additional ingredients encourage more nutrient consumption and may induce overeating but it appears that food that is minimally satiating would have the same effect.[53,93] Again, we can refer to Tseng [104] who demonstrated 24% reduction in food costs with ingredients bought from the grocery store versus consistent fast food consumption. It is important to disclose that Julie Jones works for the Grains Food Foundation, Quaker Oats Advisory Board, Campbell Soup Company Plant, and Healthy Advisory Board and thus has strong financial interest in the preservation of food processing guidelines that seem opaque.

Table 4. Comparison of Capturing Dietary Shares of the Processed Foods by IFIC and NOVA as a Percentage of Calories

Category from IFIC	Eicher-Miller[a]	Category from NOVA	Martinez-Steele[b]
Minimally Processed	14.1	**Category 1**	30.2
Foods Processed for Preservation	2.8	**Category 2**	2.9
Mixtures of Combined Ingredients	16.8	**Category 3**	9.3
Ready to Eat Foods	34.4	**Category 4**	57.5
Prepared Foods/Meals	31.9		
Total Calories	2140	**Total Calories**	2069.9

[a] The contribution of energy intake as percentage of total calories from NHANES Data[103]
[b] The contribution of energy intake as percentage of total calories from NHANES Data[52]

From the Monteiro (2017) paper, the UN Decade of Nutrition came from the evident multiple worsening threats to food systems and supplies, and thus food security, human health and welfare, living and physical world, and biosphere.[92] Food processing addresses nutrition at

the heart of sustainable development. This includes the major concern for middle- and lower-income countries that as soon as obesity rates take hold, they are expected to climb to alarming rates by 2035 in places such as Africa and Southeast Asia. To date, no other country has been able to stave off obesity as a public health issue. Because of the NOVA guidelines, organizations such as WHO, PAHO, and FAO have all been able to agree on a solid definition of what constitutes an "ultra-processed" in direct contradiction to Gibney. Monteiro's five reasons to emphasize food processing include the following. First, conventional food classifications no longer work well; they usually group foods and foodstuffs in terms of botanical origin or animal species. For example, grouping whole grains with sugared breakfast cereals under cereal and cereal products is nonsensical from a nutrient standpoint. Second, evidence on the relationship between food processing and health outcomes is increasing steadily. Americans are not looking at this as other countries have been. Third, food systems and supplies are changing globally and are determining changes in food purchase and consumption. Specialist food retailers are being rapidly displaced by supermarkets. Home cooking has decreased in favor of snacking on ready-to-eat food and the food is available round the clock. Fourth, all these phenomena are being driven by transnational corporations, which are deregulated and thus have the freedom to spend on new technology, marketing, and so on that governments do not have. They have unlimited money to spend on marketing, accounting, advertising, promotion, lobbying, manufacturing, i.e., Coca Cola and Nestlé, which were among the top ten largest global advertisers in 2014, together spending 6.2 billion, equivalent to two thirds of the entire overseas UK budget. Food processing as such is not the issue, unlike what Gibney seemed to be stating. The term *processing* is very general and not helpful. Monteiro argued that NOVA proposes more helpful definitions of processing and not all processing is inherently bad. Certainly, choice within a category matters.

Having an agreed-upon definition to determine what those choices should look like based on evidence can only come from guidelines such as NOVA. The lack of having a systematic and extensive method of measuring food processing will continue to breed mixed results in the literature and sow doubt in the public. Thus, this researcher hoped to add to the literature which has already addressed some of the criticisms and concerns related to using NOVA with objectivity, investigate health implications of maternal ultra-processed food intake on the neonate in the context of body composition using precise instrumentation, and add to the literature regarding comparison of NOVA to other measures of diet quality by asking the following questions:

- Does using the lens of NOVA increase a vocabulary to describe diet quality?
- Is there relationship between excessive gestational weight gain and maternal diet quality as measured by NOVA?
- Is there a relationship between neonatal adiposity and maternal diet quality measured by NOVA?

Aim 1: Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

1a. Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

Compared to the UC group, mothers in the LI group will have increased percentages of unprocessed food and decreased percentages of ultra-processed foods.

1b. Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

As dietary shares of ultra-processed foods increase, HEI overall scores will decrease.

1c. Compare pre and post ultra-processed food shares of the diet to the pre and post HEI overall scores controlling for calorie intake.

These correlations will weaken when controlling for overall calorie consumption as a covariate.

Aim 2: Investigate the relationship between gestational weight gain and diet quality as measured by NOVA.

2a. Examine whether the independent variable, diet quality as measured by consumption of foods categorized by NOVA as ultra-processed, has an effect on the GWG experience for mothers in both LI and UC related to Post intervention intake of ultra-processed foods adjusted for weight of food and adjusted for total energy intake.

The odds of excessive GWG will be higher for women who had higher UPF intake for both groups.

Aim 3: Investigate the relationship between maternal diet quality as measured by NOVA and neonatal body composition and compare the results of the two anthropometric measures.

3a. Investigate an association between the group differences in maternal diet quality related to ultra-processed food intake as measured by NOVA and neonatal lean mass as measured by QMR.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal lean mass as measured by QMR.

3b. Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal fat-free mass as measured by PEAPOD.

Chapter III

METHODS

The current study aimed to answer questions surrounding maternal diet quality and its impact on gestational weight gain and neonatal adiposity using the NOVA guidelines as a lens of assessment. The following are the research questions and specific aims with hypotheses:

- Does using the lens of NOVA increase a vocabulary to describe diet quality?
- Is there relationship between excessive gestational weight gain and maternal diet quality as measured by NOVA?
- Is there a relationship between neonatal adiposity and maternal diet quality measured by NOVA?

Aim 1: Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

1a. Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

Compared to the UC group, mothers in the LI group will have increased percentages of unprocessed food and decreased percentages of ultra-processed foods.

1b. Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

As dietary shares of ultra-processed foods increase, HEI overall scores will decrease.

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Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal lean mass as measured by QMR.

3b. Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal fat-free mass as measured by PEAPOD.

Study Setting

The current study, a secondary data analysis, is an ancillary study to the Lifestyle Intervention For Two (LIFT) study, which is being conducted at the New York Obesity Nutrition Research Center at Columbia University Medical Center. This chapter details how the current research study was conducted. Since this is a secondary analysis of data collected for the LIFT study, a description of the dataset and how data were collected is provided.

Source of the Data

LIFE-Moms is an NIH-sponsored consortium which leverages a Researching Coordinator Unit to deliver RCTs of Lifestyle Intervention for Two, LIFT, in seven communities across the United States. While the program specifics of each LIFT implementation vary, they collectively focus on strategies for reducing gestational weight gain in women with overweight or obesity.[22]

The LIFT (Parent) Study

Study design and statistical procedures. The LIFT study (parent study) used a parallel group randomized-controlled trial design to investigate the impact of a maternal lifestyle intervention on neonatal body composition focused on reducing gestational weight gain in women with overweight or obesity. Using collected data from the laboratory [113] on 306 infants and their mothers, an analysis was conducted to estimate the effect size for the intervention and determine the necessary sample size for LIFT study sample size assuming a type I error of 5% 2-sided and power of 80%.[22] Researchers then randomized 105 women to each of the two arms of

the LIFT study, UC and LI, which allowed for approximately 10% loss to follow-up, where the term *lost to follow-up* defined an individual who cannot be located or assessed. It was also expected that miscarriage would be minimal but that some of the births will be too premature to be assessed (for example, less than 35 weeks of gestation).

LIFT Participant Eligibility

LIFT compared body composition of newborns to mothers with overweight or obesity randomly assigned at a 1:1 ratio at the beginning of the second trimester to LI designed to control GWG to UC. The primary LIFT hypothesis was that percent body fat would be less for neonates from LI than from UC mothers. Women were recruited from hospital-affiliated private and clinic practices from February 2013 to October 2015. Eligibility criteria are listed below in Table 5.

Recruitment and Enrollment

The LIFT study used a convenience sampling strategy and recruiters at the Obstetrics Department at Mount Sinai Roosevelt Hospital to identify potential participants. Recruiters explained the study to expectant mothers who attended the Clinic, and for those women who indicated interest, a verbal consent was solicited to conduct a pre-screen. Pre-screen form and candidates contact details were provided to the LIFT Staff, who then followed up with the candidates. LIFT Staff then provided a more detailed explanation of the study and confirmed the pre-screen answers. Based on this information, eligible potential participants were invited to attend the LIFT Clinic, to obtain consent and undergo full screening procedures.

Table 5. Eligibility Criteria in LIFT

Inclusion Criteria	Exclusion Criteria
• age equal or greater than 18 • BMI of 25 or greater at baseline • singleton pregnancy • gestational age between 9,0 (week, day) and 15,6 confirmed by dating ultrasound and intention to deliver at SLRH.	• diabetes • fetal abnormality • planned termination of pregnancy • history of three or more consecutive first trimester miscarriages • current eating disorder • actively suicidal • prior or planned bariatric surgery • current use of metformin, systemic steroids, antipsychotic agents, anti-seizure medications, mood stabilizers, or ADHD medications • continued use of weight loss medications • contraindications to aerobic exercise in pregnancy • participation in another intervention study that influenced weight control • enrollment in this trial in a previous pregnancy • unwillingness or inability of the subject to commit to a 1-year follow up of herself or her child • smoking • history of drug or alcohol addiction • chronic health problems that prohibited regular exercise known to influence body composition • claustrophobia • lack of support from primary health care provider or family members • having another member of the household a study participant or staff member • any other medical, psychiatric, social or behavioral factor that in the judgments of the study principal investigators might interfere with study participation or ability to follow the intervention

Informed Consent Process

All screening and testing procedures as well as risks and benefits of participation were explained in detail to the mothers, both orally and in writing. An explanation of the risks associated with the study and information on confidentiality of the data acquired were provided. Questions were asked and answers elicited in order to ascertain that participants comprehend the study procedures as well as potential risks involved prior to consenting to participation. When subject questions were answered by the research staff, written informed consent was obtained from the subject and witnessed by a third party. All subjects were required to give informed consent/assent prior to their participation in the study. Consenting procedures were HIPAA-compliant. Study participants were explicitly told that their participation at all stages of the study was entirely voluntary, that they were free to discontinue participating at any time, and that there may be no direct benefits to them from participation. All participants were required to sign a HIPAA-compliant medical records release at baseline before randomization into the study.

Research Setting

Procedures were completed at the LIFT Study offices located in Manhattan, New York. The physical sites included: LIFT Study, Columbia University, 1790 Broadway; LIFT Study/Columbia University—Body Composition Unit, 21 Audubon Avenue; and LIFT Study/QMR lab, Mt. Sinai West (formerly St. Luke's Roosevelt Hospital), 1000 Tenth Avenue. If participants were unable to complete their postpartum visits at the locations listed, some postpartum procedures (see below) were completed at the participants' home by certified study staff.

Data Collection

Data were collected at multiple points throughout the parent study. At prescreen, a preliminary screen was completed on interested candidates to determine eligibility at the clinical site and to eliminate obviously ineligible volunteers (verbal consent for this procedure). The pre-screen forms were passed to the LIFT Research Coordinator who contacted the interested subjects to provide candidates with further information about the study. Candidates' questions were answered and the answers to the pre-screen questionnaire confirmed. Eligible subjects were invited to attend a formal screening and consent visit (SV1), ineligible subjects were informed that they were not eligible to participate in the study and they would not be contacted any further.

Table 6. Participant Measures Collected at Pre Intervention (Week 14 Gestational Age) and Intervention

Screening Visit 1	Screening Visit 2	Intervention Visits
Anthropometric measures	Baseline **Maternal Measures**: • Body weight • Anthropometric and skinfold measurements • Blood pressure • Body composition • Whole Body MRI (optional) • Echo MRI (QMR) • BodPod • Blood draw • Urine sample • Dietary intake assessment • Physical activity/sleep monitoring • Current medications • Contraindications to exercise • Sedentary behavior item • Physical activity item • Frequency of self-weighing • Modified EDEQ [114] • BDI-II [115] • SF-12 • NuMoms2B sleep • Mindful Eating questionnaire	ASA24 Food Logs Maternal weights
Behavioral interview	Randomization	
HbA1C	Initial Counseling	

Additional follow-up study visits for data collection purposes (not intervention visits), procedures as described for baseline measurements, were scheduled for all participants (both ILI and UC group) at the following time points, as shown in Table 7.

Table 7. Participant Measures Collected at Post Intervention (Week 35 Gestational Age) and At Delivery/Infant

Post Intervention Measures	Delivery and Infant Measures[a]
Maternal Measures: • Body weight • Anthropometric and skinfold measurements • Blood pressure • Body composition • Whole Body MRI (optional) • Echo MRI (QMR) • BodPod • Blood draw • Urine sample • Dietary intake assessment • Physical activity/sleep monitoring • Questionnaires • Current medications • Contraindications to exercise • Sedentary behavior item • Physical activity item • Frequency of self-weighing • Modified EDEQ [114] • BDI-II [115] • SF-12 • NuMoms2B sleep • Mindful Eating questionnaire	**Infant Measures:** • Infant body weight • Infant body measurements: • Length • Head circumference • Skinfold measurements at triceps, thigh and subscapular • Body Composition: • Infant Echo MRI (QMR) • PEAPOD • Other measurements: Cord blood sample and placenta samples (both are optional)

[a] Measures collected while mother and child are inpatient at Roosevelt hospital following delivery

Following patient discharge, information was collected from Medical Records on the delivery and health of the newborn.

Study Intervention Design

Following the collection of the baseline measurements, participants were randomized at the end of the second clinic visit to one of the two study arms, *Usual Care* (UC) or *Lifestyle Intervention (LI)*, using a random number generator to generate the sequence of treatment assignments. The SAS (statistical analysis system, computer program) was used to generate a

random number by means of the RANUNI function. Each potential subject was assigned a number in the order they were generated. The subjects were assigned by the following rule: If the random number (between 0 and 1) was less than .5, assign subject to group A, if greater than or equal to .5, assign to group B. The parent study used simple randomization without blocks or stratification for this study. Some data collection procedures were designated to be collected by blinded staff to the extent feasible.

Usual Care Group (UC)

Participants randomized to UC received basic education on healthy eating using MyPlate for Pregnancy and Breastfeeding from the USDA Center for Nutrition Policy (http://www.mypyramid.gov/mypyramidmoms/index.html) and the Nutrition Care Manual (Academy of Nutrition and Dietetics, http://nutritioncaremanual.org/index.cfm). Counselors reviewed weight gain recommendations for pregnancy based on the IOM 2009 report. Participants were advised to avoid alcohol consumption and smoking and to adopt and maintain an active lifestyle. Materials recommended ways gradually to increase physical activity (PA) (e.g., using stairs vs. elevators, walking vs. transport, etc.), ultimately reaching the recommended activity goal of at least 30 minutes per day, 5 days per week.

UC received one 20-minute session at the randomization visit. After this session, UC was invited to group meetings every 8 weeks during pregnancy, then 3 times total during the 1-year post-partum period. These groups were based on the wellness curriculum designed for the LA Diabetes Support and Education (DSE) group, modified for a non-diabetic, pregnant population. The LIFT groups were informative and designed to promote retention of the UC. If necessary, due to enrollment, pregnant and post-partum groups were combined. With the exception of

routine visits to her prenatal care provider and the RCT visits described above, there was no other RCT intervention for UC participants.

Intensive Lifestyle Intervention (LI)

LI combined diet modification, increased physical activity, and behavioral change with the goal of controlled gestational weight gain (GWG). Information related to safety of controlled weight gain in overweight/obese pregnant individuals is presented below. LI was a counseling program based on individual sessions, derived from the group behavioral programs developed for the treatment of overweight/obese patients in the Diabetes Prevention Program (DPP) and the Look AHEAD Study (LA).[117,118] The focus in LIFT LI had been adjusted from weight loss to controlled GWG based on the IOM 2009 treatment guidelines. The physical activity goal was to increase caloric expenditure by at least of 700 kcal/wk (100 kcal/day) through moderate exercise, following ACOG guidelines for exercise during pregnancy. Counselors utilized MyPlate for Pregnancy and Breastfeeding from the USDA Center for Nutrition Policy (http://www.choosemyplate.gov/mypyramid/mpm/index.hml and the Nutrition Care Manual (Academy of Nutrition and Dietetics, http://nutritioncaremanual.org/index.cfm) as the basis for nutrition counseling. Participants' calorie intake was adjusted according to their pre-pregnancy BMI and gestational trimester. Counselors utilized meal plans to emphasize a nutrient-dense diet, with calories adjusted for the changing needs of pregnancy. Materials included a weight chart and advice regarding the benefits of appropriate GWG.[113,119]

A multi-component intervention was used, including diet modification, physical activity, behavioral strategies, and social support via weekly individual counseling sessions. Two additional contacts per week, either via email or telephone, provided further support.

A curriculum manual was developed by LIFT staff that included an individualized component designed to enable the Case Manager to provide flexible and timely information to the participant. This flexibility was an integral component of the LI. Because of the evolving nutritional needs of pregnancy, the curriculum easily adjusted to the unique needs of each participant (depending on trimester, lifestyle, ethnicity, season of the year, etc.). Materials were designed to be appropriate for individuals of different ethnic backgrounds and education levels. The highly trained counselors had extensive experience in weight loss/weight management counseling and were skilled nutrition counselors and educators. In addition to the strategies discussed here, advanced behavioral techniques were offered to promote controlled GWG. These included cognitive restructuring and mindfulness-based approach to behavioral change.

From the data collected in the LIFT parent study, the current study focused on dietary intake data, gestational weight gain, and neonatal body composition measured at weeks 14, 35, and delivery, respectively.

Current Study

The current study was a secondary analysis of data collected in the LIFT study using the ASA-24 recall which was administered to study participants at weeks 14 and 35 during pregnancy. The data included were limited to those who completed ASA-24 recalls at pre intervention and post intervention, where the recall was visually checked for completeness and reported by the participant as being representative of typical intake. Data collected at week 14 were used as pre-intervention food intake and at week 35 as post-intervention food intake. To compare results, it is most meaningful to look these time points where intakes are reported as typical of usual intake. The current study focused on the intake of ultra-processed foods as measured by NOVA and their impact upon gestational weight gain trajectories between the two

groups and neonatal body composition post-intervention. Maternal weights at Pre intervention and Post intervention allowed for the calculation of weight gain; neonatal adiposity 1-3 days birth after birth, measured by two independent methods—air displacement plethysmography and quantitative magnetic resonance imaging, were included for regression models looking at relationships between ultra-processed food intake and body composition.

Table 8. Study Variables, Type, Data Source, Description, Rationale

Variable	Type	Data Source	Description	Rationale
Percentages of NOVA categories 1 and 2 adjusted for weight of food in grams and adjusted for contribution of energy intake in kilocalories for pre and post intervention recalls	Predictor, ratio	ASA24	Each participant receives a NOVA categories 1 and 2 score provided via ASA24 information and established NOVA group assignment methodology	To make comparison more fluid with HEI score
Percentages of NOVA category 4 adjusted for weight of food in grams and adjusted for contribution of energy intake in kilocalories for pre and post intervention recalls	Predictor, ratio	ASA24	Each participant receives a NOVA categories 1 and 2 score provided via ASA24 information and established NOVA group assignment methodology	To make comparison more fluid with HEI score
Overall HEI score	Dependent, continuous	HEI	A 0-100 score based on twelve categories of food groups	Established measure of diet quality used in parent study
Excessive GWG (Weight)	Dependent, categorical	LIFT	A dummy variable to determine if participant gained excessively, 1= yes, 0=no	To address probability of low, med, or high ultra processed food intake and excessive GWG, targeted in intervention by calories via MyPlate
PeaPod (Fat free mass in grams) QMR (Total lean mass in grams)	Dependent, continuous	LIFT	Grams of FFM for neonates	Most precise and validated measures to look at impact of maternal intake of ultra processed processed foods on fetal lean mass programming

Instrumentation

This study used the ASA 24, weight (SECA), the Healthy Eating Index (HEI), neonatal adiposity by QMR and ADP (PEAPOD), and the NOVA guidelines.

Table 9. Instrumentation

Instrument	What it Measures	Rationale
ASA 24	24 hour food intake	Ability to best calculate actual intake
HEI	Diet quality according to Dietary Guidelines	Validated for population
QMR	Body composition via hydrogen ion status	Validated for population
PEAPOD	Body composition via air displacement	Validated for population
NOVA Guidelines	Dietary pattern of ultra processed and unprocessed food intake	Outside of IFIC, currently only tool to measure extent of processing only with regard to dietary patterns

The ASA24. The ASA24 is composed of two web-based applications—a Respondent Website and a Researcher Website. The Respondent Website uses a dynamic interface to complete a 24HR recall from the previous 24 hours. The dynamic interface includes an animated guide, audio and video, to guide participants through the recording of their eating occasions and includes data collection on both food and behavior associated with each eating occasion. This 24HDR is based upon the USDA Automated Multiple Pass Method (AMPM), which has been validated and shown to accurately estimate mean total energy and protein intakes compared to recovery biomarkers.[119] The Researcher Website provides access to nutrient and food group analyses to researchers, nutritionists, and educators, and also allows for the management of logistics of data collections and data file procurement. Researchers can obtain a variety of reports based on the FNDDS and modify the data collected per each eating occasion.

The Healthy Eating Index-2010. The Healthy Eating Index (HEI) is a diet quality index that measures conformance with federal dietary guidance. The HEI is used for a variety of applications including population monitoring, epidemiologic research, and evaluations of the food environment, food assistance packages, nutrition interventions, and the relation between diet cost and diet quality.[120] The HEI includes 12 components, nine of which assess adequacy of the diet including (a) total fruit, (b) whole fruit, (c) total vegetables, (d) greens and beans, (e) whole grains, (f) dairy, (g) total protein foods, (h) seafood and plant proteins, and (i) fatty acids. The remaining three—refined grains, sodium, and empty calories—assess dietary components that should be consumed in moderation. For all components, higher scores reflect better diet quality. Scoring is tallied as follows:

Table 10. The HEI 2010 Scoring System

HEI -2010 Component	Maximum	Standard for Maximum	Standard for minimum
Adequacy (higher score indicates higher consumption)			
Total Fruit	5	>.8 cup equiv/1000kcal	No fruit
Whole Fruit	5	>.4 cup equiv/1000kcal	No whole fruit
Total Vegetables	5	>1.1 cup equiv/1000kcal	No vegetables
Greens and Beans	5	>.2 cup equiv/1000kcal	No dark green vegetables beans or peas
Whole Grains	10	>1.5 oz equiv/1000kcal	No whole grains
Dairy	10	>1.3 cup equiv/1000kcal	No dairy
Total Protein Foods	5	>2.5 oz equiv/1000kcal	No protein
Seafood and Plant Protein	5	>.8 oz equiv/1000kcal	No seafood or plant protein
Fatty Acids	10	>PUFAs + MUFAs)/SFAs > 2.5	(PUFAs + MUFAs)/SFAs < 1.2
Moderation (higher score indicates lower consumption)			
Refined Grains	10	<1.8 oz equiv/1000kcal	>4.3 oz equiv/1000kcal
Sodium	10	<1.1g equiv/1000kcal	>2 g/1000 kcal
Empty Calories	20	<19% total energy	>50% total energy

The HEI has been validated [120] and correlates highly with measured energy intake.

NOVA guidelines. Developed by Carlos Monteiro and colleagues at the University of Sao Paulo, Brazil in 2009, the NOVA guidelines have been used extensively in assessing shares

of ultra-processed foods at the national level in several countries and several studies have reported on observed associations with various suboptimal metabolic states in various special populations.[43-46,52,94-97,101,102,110,112]

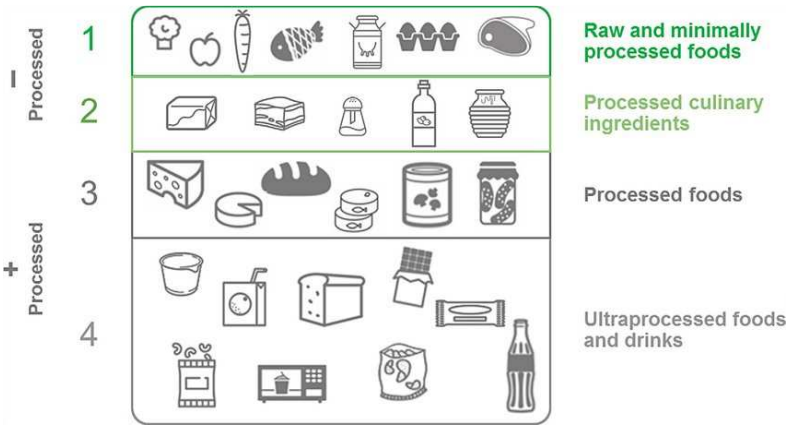

Figure 4. The NOVA guidelines

Previous publications have used a method to classify foods into NOVA categories [52,101,102] that utilize food codes from the FNDDS (Food and Nutrient Databases for Dietary Studies) that are included in the ASA24 data. Nine-digit food codes and their underlying ingredient codes (SR or standard reference codes) are used to determine which part of the food item will be assigned to the NOVA categories. The first three to five digits of the food code determines NOVA category; if the food is more complex requiring additions of foods or is determined to be a handmade recipe, the underlying ingredient codes may be used. For example, the item listed as a Milk-based meal replacements, fluid would be categorized as a Category 4 Food; Subgroup "Milk-based drinks" if the food code =11560020. This relays information that the milk-based meal replacement is ready for consumption as sold. However, if the food code = 11612000, this indicates that the consumer must add milk to the product, classifying it as a combination food; some of the product will be allocated to group 4 and some of the product will be allocated to category 1. The energy content and weight of foods reported in the ASA24 are derived using the

FNDDS 4.1 along with the SR release 22 for quantifying percentage of energy intake and percentage of food weight along with identification of the NOVA category. STATA SE14 was used for this portion of the data analysis.

Table 11. NOVA food groups: definition according to the extent and purpose of food processing, with examples* [121]

NOVA group	Definition	Examples
1) Unprocessed or minimally processed foods	Unprocessed: edible parts of plants (fruits, seeds, leaves, stems, roots, tubers) or of animals (muscle, offals, eggs, milk), and also fungi, algae and water, after separation from nature. Minimally processed: unprocessed foods altered by industrial processes such as removal of inedible or unwanted parts, drying, crushing, grinding, fractioning, roasting, boiling, pasteurisation, refrigeration, freezing, placing in containers, vacuum packaging, non-alcoholic fermentation, and other methods that do not add salt, sugar, oils or fats or other food substances to the original food. The main aim of these processes is to extend the life of unprocessed foods, enabling their storage for longer use, and, often, to make their preparation easier or more diverse. Infrequently, minimally processed foods contain additives that prolong product duration, protect original properties or prevent proliferation of microorganisms.	Fresh, squeezed, chilled, frozen, or dried fruits and leafy and root vegetables; grains such as brown, parboiled or white rice, corn cob or kernel, wheat berry or grain; legumes such as beans, lentils, and chickpeas; starchy roots and tubers such as potatoes, sweet potatoes and cassava; fungi such as fresh or dried mushrooms; meat, poultry, fish and seafood, whole or in the form of steaks, fillets and other cuts, fresh or chilled or frozen; eggs; fresh or pasteurized milk; fresh or pasteurised fruit or vegetable juices (with no added sugar, sweeteners or flavours); grits, flakes or flour made from corn, wheat, oats, or cassava; tree and ground nuts and other oily seeds (with no added salt or sugar); herbs and spices used in culinary preparations, such as thyme, oregano, mint, pepper, cloves and cinnamon, whole or powdered, fresh or dried; fresh or pasteurized plain yoghurt; tea, coffee, and drinking water. Also includes foods made up from two or more items in this group, such as dried mixed fruits, granola made from cereals, nuts and dried fruits with no added sugar, honey or oil; pasta, couscous and polenta made with flours, flakes or grits and water; and foods with vitamins and minerals added generally to replace nutrients lost during processing, such as wheat or corn flour fortified with iron and folic acid.
2) Processed culinary ingredients	Substances obtained directly from group 1 foods or from nature by industrial processes such as pressing, centrifuging, refining, extracting or mining. Their use is in the preparation, seasoning and cooking of group 1 foods. These products may contain additives that prolong product duration, protect original properties or prevent proliferation of microorganisms.	Vegetable oils crushed from seeds, nuts or fruits (notably olives); butter and lard obtained from milk and pork; sugar and molasses obtained from cane or beet; honey extracted from combs and syrup from maple trees; starches extracted from corn and other plants, and salt mined or from seawater, vegetable oils with added anti-oxidants, and table salt with added drying agents. Includes products consisting of two group 2 items, such as salted butter, and group 2 items with added vitamins or minerals, such as iodised salt.

3) Processed foods	Products made by adding salt, oil, sugar or other group 2 ingredients to group 1 foods, using preservation methods such as canning and bottling, and, in the case of breads and cheeses, using non-alcoholic fermentation. Processes and ingredients here aim to increase the durability of group 1 foods and make them more enjoyable by modifying or enhancing their sensory qualities. These products may contain additives that prolong product duration, protect original properties or prevent proliferation of microorganisms.	Canned or bottled vegetables and legumes in brine; salted or sugared nuts and seeds; salted, dried, cured, or smoked meats and fish; canned fish (with or without added preservatives); fruits in syrup (with or without added anti-oxidants); freshly made unpackaged breads and cheeses.
4) Ultra-processed foods	Formulations of ingredients, mostly of exclusive industrial use, that result from a series of industrial processes (hence 'ultra-processed'), many requiring sophisticated equipment and technology. Processes enabling the manufacture of ultra-processed foods include the fractioning of whole foods into substances, chemical modifications of these substances, assembly of unmodified and modified food substances using industrial techniques such as extrusion, moulding and pre-frying, frequent application of additives whose function is to make the final product palatable or hyper-palatable ('cosmetic additives'), and sophisticated packaging, usually with synthetic materials. Ingredients often include sugar, oils and fats, and salt, generally in combination; substances that are sources of energy and nutrients but of no or rare culinary use such as high fructose corn syrup, hydrogenated or interesterified oils, and protein isolates; cosmetic additives such as flavours, flavour enhancers, colours, emulsifiers, sweeteners, thickeners, and anti-foaming, bulking, carbonating, foaming, gelling, and glazing agents; and additives that prolong product duration, protect original properties or prevent proliferation of microorganisms. Processes and ingredients used to manufacture ultra-processed foods are designed to create highly profitable products (low cost ingredients, long shelf-life, emphatic branding), convenient (ready-to-consume) hyper-palatable snacked products liable to displace all other NOVA food groups, notably group 1 foods.	Carbonated soft drinks; sweet or savoury packaged snacks; chocolate, candies (confectionery); ice-cream; mass-produced packaged breads and buns; margarines and other spreads; cookies (biscuits), pastries, cakes, and cake mixes; breakfast 'cereals', 'cereal' and 'energy' bars; 'energy' drinks; milk drinks, 'fruit' yoghurts and 'fruit' drinks; 'cocoa' drinks; 'instant' sauces; infant formulas, follow-on milks, other baby products; 'health' and 'slimming' products such as meal replacement shakes and powders. Many ready to heat products including pre-prepared pies and pasta and pizza dishes; poultry and fish 'nuggets' and 'sticks', sausages, burgers, hot dogs, and other reconstituted meat products, and powdered and packaged 'instant' soups, noodles and desserts.

* Alcoholic drinks are not immediately classifiable by NOVA. By analogy with the nature of processed and ultra-processed foods, they may be counted in group 3 if they are produced by fermentation of group 1 foods, such as beer, cider, and wine, and in group 4 if they are produced by fermentation of group 1 foods and distillation of the resulting alcohol, such as whisky, gin, rum, and vodka. Another option, depending on why NOVA is being used, is to treat alcoholic drinks separately.

Anthropometric measures (GWG, PEAPOD, and QMR). Gestational weight gain was measured using a Tanita (BWB-800, Tanita Corp., Arlington Heights, Illinois) scale. Weight gain rate was labeled as adequate or excessive per IOM guidelines.[4]

The PEAPOD Infant Body Composition System (COSMED USA Inc., Concord, California) is an infant-sized air displacement plethysmography system that directly measures infant bodyweight and volume and uses these values to derive body fat percentage, fat mass, and fat-free mass.[122] This system has been validated in infants against the gold standard four-compartment model and deuterium dilution.[123]

As aforementioned, the criterion method to measure body composition is the four-compartment model; this technique requires several instruments and is cumbersome. A recent advance in technology, the quantitative nuclear magnetic resonance has been validated in animals and adults.[124] However, when validated against deuterium dilution and the four-compartment model, the QMR requires some mathematical adjustments to replicate those methods' results in the population of neonates. This method takes advantage of the properties of hydrogen atom in organic and inorganic environments to differentiate signals from fat or lean tissue and has been validated for use in neonates.[125]

Data Analysis

The following section introduces each aim from Chapter I with a clear plan and hypotheses to follow. All data were analyzed using SPSS v25.

Aim 1: Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

1a. Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

Compared to the UC group, mothers in the LI group will have increased percentages of unprocessed food and decreased percentages of ultra-processed foods.

1b. Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

As dietary shares of ultra-processed foods increase, HEI overall scores will decrease.

1c. Compare pre and post ultra-processed food shares of the diet to the pre and post HEI overall scores controlling for calorie intake.

These correlations will weaken when controlling for overall calorie consumption as a covariate.

Aim 1 Data Analysis Plan: T tests and Correlations

To describe the diet, the investigator first calculated percentages of dietary contribution as described above for the selected NOVA category for each group and for each time point. Using t-tests, the investigator tested for between-group differences. Additional analysis included Pearson correlations to test for associations between groups and participants. Tests of assumptions were performed and reported. For many of the statistical analyses conducted in this study, the investigator met the assumptions of each model having one dependent variable that is measured at the continuous (ratio or interval) level. Other assumptions included normal distribution of the differences in the dependent variables. In addition to reliance on the Central

Limit Theorem, a Shapiro-Wilk test of normality and Q-Q plots were conducted to ascertain this assumption was met. For the t-test, the null hypothesis was that, H_0: the population mean difference between the values is equal to zero (i.e., $\mu_{diff} = 0$), and the alternative hypothesis (H_A) was: the population mean difference between the values is not equal to zero (i.e., $\mu_{diff} \neq 0$).[126-131]

The Pearson product-moment correlation was used to determine the strength and direction of a linear relationship between two continuous variables. More specifically, the test generated a coefficient called the Pearson correlation coefficient, denoted as *r* (i.e., the italic lowercase letter r), and this coefficient measures the strength and direction of a linear relationship between two continuous variables. Its value can range from -1 for a perfect negative linear relationship to +1 for a perfect positive linear relationship. A value of 0 (zero) indicates no relationship between two variables. To run a Pearson's correlation, five assumptions need to be considered. The first assumption is that the two variables should be continuous, and the variables should be paired. Third, there needs to be a linear relationship between the two variables. The investigator checked this assumption by plotting a scatterplot and visually inspecting the graph. Fourth, there should be no significant outliers**.** Pearson's correlation coefficient, *r*, is sensitive to outliers, meaning that outliers can have an exaggerated influence on the value of *r*. This can lead to Pearson's correlation coefficient not having a value that best represents the data as a whole. The investigator also needed to test for normality using the Shapiro-Wilk test. The null hypothesis for this test was as follows: H_0: $\rho = 0$; the population correlation coefficient is equal to zero. The alternative hypothesis was: H_A: $\rho \neq 0$; the population correlation coefficient is not equal to zero.[126-131]

Aim 2: Investigate the relationship between gestational weight gain and diet quality as measured by NOVA.

2a. Examine whether the independent variable, diet quality as measured by consumption of foods categorized by NOVA as ultra-processed, has an effect on the GWG experience for mothers in both LI and UC related to Post intervention intake of ultra-processed foods adjusted for weight of food and adjusted for total energy intake.

The odds of excessive GWG will be higher for women who had higher UPF intake for both groups.

Aim 2 Data Analysis Plan: Binomial Logistic Regression (Odds Ratio)

A binomial logistic regression attempts to predict the probability that an observation falls into one of two categories of a dichotomous dependent variable based on one or more independent variables that can be either continuous or categorical. To run a binomial logistic regression, the following requirements must be met: (a) outcome variable must be dichotomous, either adequate or excessive GWG; (b) independent variables must be continuous; (c) observations must be independent; (d) categories of the dichotomous dependent variable and the minimal independent variable must be mutually exclusive; (e) must be a minimum of 15 cases per independent variable; and (f) a linear relationship between the continuous independent variables and the logit transformation of the dependent variable must exist.

The investigator used the Box-Tidwell approach, which adds interaction terms between the continuous independent variables and their natural logs to the regression equation. The data must not show multicollinearity. Multicollinearity occurs when there two or more independent variables that are highly correlated with each other. This leads to problems with understanding which independent variable contributes to the variance explained in the dependent variable, as

well as technical issues in calculating a binomial logistic regression model. The investigator inspected correlation coefficients and Tolerance/VIF values to detect for multicollinearity. The investigator ran tests in SPSS to check for here significant outliers, high leverage points, or highly influential points.[126-131]

Hypothesis: $\text{logit}(Y) = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_4X_4 + e$

Aim 3: Investigate the relationship between maternal diet quality as measured by NOVA and neonatal body composition and compare the results of the two anthropometric measures.

3a. Investigate an association between the group differences in maternal diet quality related to ultra-processed food intake as measured by NOVA and neonatal lean mass as measured by QMR.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal lean mass as measured by QMR.

3b. Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal fat-free mass as measured by PEAPOD.

Aim 3 Data Analysis Plan: Linear Regression

A simple linear regression assesses the linear relationship between two continuous variables to predict the value of a dependent variable based on the value of an independent variable. More specifically, the investigator used this method to determine whether the linear regression between these two variables was statistically significant, determine how much of the variation in the dependent variable was explained by the independent variable, understand the direction and magnitude of any relationship; and predict values of the dependent variables based on different values of the independent variable. The same assumptions regarding the variables must be met as stated in the last two questions. In addition, (a) a linear relationship must exist between the variables, (b) observations must be independent, (c) homoscedasticity must exist, (d) no significant outliers, and (e) the residuals of the regression line are approximately normally distributed. A scatterplot was examined to determine if the linear relationship existed. A Durbin Watson statistic was checked to ensure independence of observations. If the residuals were not independent, they were often referred to as correlated. Having independent residuals means that one residual cannot provide information about another residual. A lack of independent errors can occur if there are improvements or detriments over time in how a dependent variable is measured. Outliers were examined. The assumption of homoscedasticity is an important assumption of linear regression and indicates that the variance of the errors (residuals) is constant across all values of the independent variable and can be checked using the plot. A histogram and P-P plot were used to determine normality.[126-131]

- $Y = \beta_0 + \beta_1 X + \varepsilon$

Chapter IV

RESULTS

Study Design and Descriptive Characteristics

The current study aimed to answer questions surrounding maternal diet quality and its impact on gestational weight gain and neonatal adiposity using the NOVA guidelines as a lens of assessment. The following are the specific aims with hypotheses:

Aim 1: Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

1a. Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

Compared to the UC group, mothers in the LI group will have increased percentages of unprocessed food and decreased percentages of ultra-processed foods.

1b. Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

As dietary shares of ultra-processed foods increase, HEI overall scores will decrease.

1c. Compare pre and post ultra-processed food shares of the diet to the pre and post HEI overall scores controlling for calorie intake.

These correlations will weaken when controlling for overall calorie consumption as a covariate.

Aim 2: Investigate the relationship between gestational weight gain and diet quality as measured by NOVA.

2a. Examine whether the independent variable, diet quality as measured by consumption of foods categorized by NOVA as ultra-processed, has an effect on the GWG experience for mothers in both LI and UC related to Post intervention intake of ultra-processed foods adjusted for weight of food and adjusted for total energy intake.

The odds of excessive GWG will be higher for women who had higher UPF intake for both groups.

Aim 3: Investigate the relationship between maternal diet quality as measured by NOVA and neonatal body composition and compare the results of the two anthropometric measures.

3a. Investigate an association between the group differences in maternal diet quality related to ultra-processed food intake as measured by NOVA and neonatal lean mass as measured by QMR.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal lean mass as measured by QMR.

3b. Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

Compared to the usual care group, mothers in the intervention group with less ultra-processed food intake will have a positive linear relationship with neonatal fat-free mass as measured by PEAPOD.

Study Design Flow

Maternal food recall data, covariates, neonatal body composition data, and covariates were provided by the parent study, LIFT. For that study, 10,716 individuals were assessed for

eligibility with initial and final screening excluding 10,506 individuals. The parent study randomized 210 women into the study. This secondary analysis only included in the analyses participants who had: (a) completed both pre intervention and post intervention ASA24 recalls with food codes or underlying ingredients recognized by NOVA group classification; (b) had completed both pre intervention and post intervention ASA24 recalls and PEAPOD measurements; or (c) had completed both pre intervention and post intervention ASA24 recalls and QMR measurements.

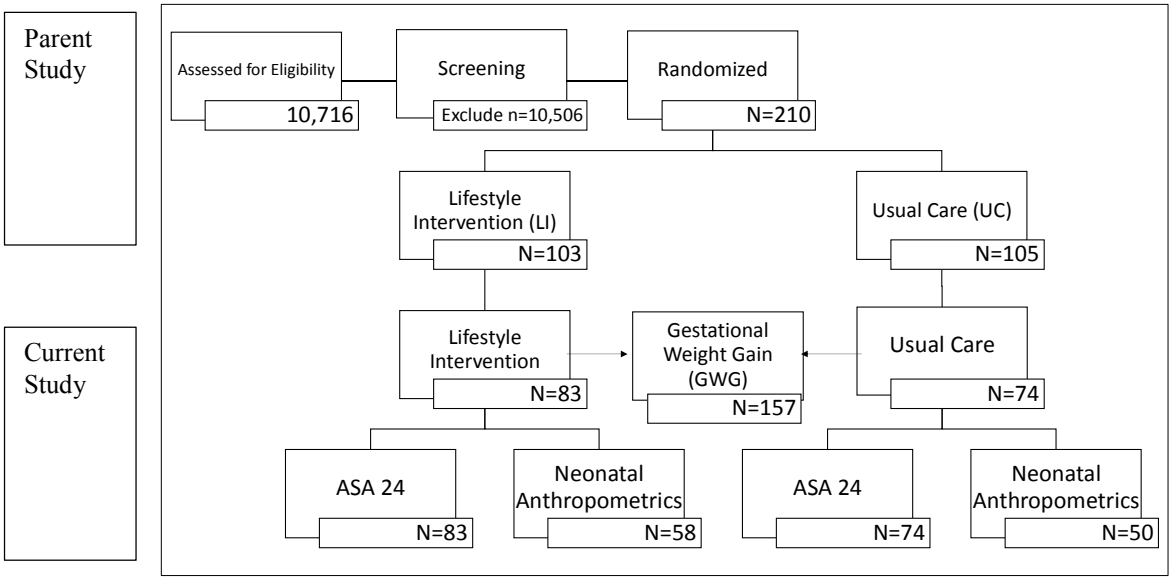

Figure 5. Consort diagram

Maternal Descriptives

All maternal pre intervention characteristics data were examined for violations of assumptions related to normal distribution, equality of variances, and potential outliers. Violations of the assumptions of normality were examined visually by histograms and Q-Q plots along with identifying any significant p values from a Shapiro Wilk test for weight, race/ethnicity, household income, and education, and are included in the appendices. Maternal descriptive variables found to be not normally distributed or with unequal variances were total calories with $p = 0.019$ for Levene's test and gestational weight gain was not normally

distributed; however, this was expected for that particular variable. Race and parity were also analyzed using chi square due to having significance for Shapiro-Wilk along with being categorical variables. Appropriate test statistics and corresponding values were reported per test assumptions. Lifestyle Intervention and Usual Care groups were not characteristically different at pre intervention for the subsample. In addition, the subsample in this secondary analysis was not different from the parent study sample at pre intervention[124-129] (see Table 12).

However, the outcomes of gestational weight gain, Healthy Eating Index (HEI) differed by group at post intervention. The mothers in the Lifestyle Intervention group experienced significantly less weight gain than the Usual Care group ($t = 2.754$, $p = .023$). In addition, there were significant improvements in the lifestyle intervention group HEI overall score which were significantly different from the average HEI score in the usual care group ($t = -2.465$, $p = .015$). The investigator also reported total calories and total PFW for each recall to frame the relatable variables chosen for the secondary analyses (see Table 13).

Neonatal Descriptives

Data were examined for violations of assumption related to normal distribution, equality of variances, and potential outliers. Neonatal covariates were distributed normally for weight and length, with the exception of outliers in the Usual Care group that contributed to a non-normal distribution in that group. Outliers were included in the final analysis as linear regression was robust to this violation (see Table 14).

Table 12. Maternal Pre intervention Characteristics for Parent Study and Secondary Analysis

Characteristics	Parent Study*		Current Study			
	LI (n=89)	UC (n=80)	LI (n=83)	UC (n=74)	Test statistic	Sig
Maternal Age (years)	33.8±4.0	33.8±4.7	33.62± 3.93	33.21 ± 4.37	-.612[a]	.542
Gestational Age at Randomization (weeks)	14.96 ± 0.72	14.82 ± 0.78	14.42 ± .751	14.43 ± .795	.087[a]	.931
Height (cm)	164.3 ± 5.4	163.5 ±7.0	164.65± 5.44	163.80 ± 6.78	-.875[a]	.383
Weight (kg)	81.5 ± 12.4	82.2±15.0	81.07 ± 12.19	83.24 ± 15.86	.966[a]	.355
Mean BMI Categories (kg/m^2) >24.9 >29.9	30.1 ±4.1 65 (62%) 40 (38%)	30.7 ±5.0 60 (57%) 45 (43%)	29.86 ± 3.88 54 (65.1%) 29 (34.9%)	31.0 ± 5.4 41 (55.4%) 33 (44.6%)	1.528[a] 1.526[c]	.129 .217
Parity 0 1 >2	 39 (37%) 30 (29%) 26 (34%)	 38 (36%) 31 (30%) 36 (34%)	 27 (32.5%) 25 (30.1%) 31 (37.3%)	 26 (35.1%) 25 (33.8%) 23 (31.1%)	.690[c]	.708
Race/Ethnicity Hispanic Non-Hispanic African American Non-Hispanic Caucasian More than one race	 32 (30%) 25 (24%) 48 (46%) ---	 25 (24%) 25 (24%) 48 (46%) ---	 25 (30.1%) 16 (19.3%) 36 (43.4%) 6 (7.2%)	 17 (23.0%) 16 (21.6%) 34 (45.9%) 7 (9.5%)	1.146[c]	.766
Household Income <$24,999 $25,000-$74,9999 >$75,000	 3 (3%) 31 (30%) 71 (67%)	 7 (7%) 29 (28%) 69 (65%)	 4 (4.8%) 27 (32.5%) 52 (62.7%)	 5 (6.8%) 20 (27.0%) 49 (66.2%)	2.065[d]	.583
College Degree No Yes	 19 (18%) 86 (82%)	 15 (14%) 90 (86%)	 17 (20.5%) 66 (79.5%)	 10 (13.5%) 64 (86.5%)	1.334[c]	.248
Pre intervention ASA24	N=89	N=80	N=83	N=74		
Total calories (Kcal)	---	---	1813.86±733.5	2088.97 ± 1067.4	1.860[a]	.065
Total PFW (g)	---	---	2976.89±1405.3	2967.68 ± 1204.7	-.044[a]	.762
HEI 2010 Score	56.34± 14.26	56.76± 16.52	56.70 ±14.22	56.09 ±16.32	-.250[a]	.803
Total Fruit	3.48±1.86	3.51±1.95	3.47±1.87	3.39±1.98	-.254[e]	.800
Whole Fruit	3.45±2.14	3.20±2.18	3.47±1.88	3.12±2.19	-1.004[e]	.317
SoFAAS	13.745 ± 5.21	13.82 ±5.96	14.06±5.07	13.51±6.01	-.618[e]	.437

*None of the tests were significant for groups at Pre intervention for parent study
a = t statistic reported, b = 2xc chi square reported, c = rx2 chi square reported, d = rx2 Fischers reported
e = Mann Whitney u distribution reported

Table 13. Maternal Outcomes After a Lifestyle Intervention

	Parent Study			Current Study			
Characteristic	Lifestyle Intervention (n = 97)	Usual Care (n = 99)	*p*	Lifestyle Intervention (n = 83)	Usual Care (n = 74)	Test Statistic	*p*
GWG Pre intervention-35	7.89 ± 4.07	9.67±4.17	.003	7.98±3.86	9.8 ± 4.4	2.754[a]	.007*
IOM GWG Adherence	---	---	.002			5.137[b]	.023*
Gained Adequately	---	---	---	51 (62.2%)	33 (44.6%)	---	---
Gained Excessively	---	---	---	31 (37.8%)	41 (55.6%)	---	---
Post Intervention ASA24	(n = 97)	(n = 99)		N = 83	N=74		
Total calories	---	---	---	1843.4±979.5	1880.7 ± 1072	.206	.837
Total PFW	---	---	---	3115.3± 1645.8	3254.2 ± 1704.5	2888[e]	.520
HEI 2010 Score	56.34± 14.26	56.76±16.52	.009	62±16	55.8 ±15.5	-2.465	.015*
Total Fruit	3.82±1.70	3.04±1.91	.0065	3.83± 1.69	3.05± 1.96	3735[e]	.009*
Whole Fruit	3.86±1.98	3.02±2.22	.0109	3.87±2	3.00±2.24	3735[e]	.004*
SoFAAS	14.37±5.78	12.56±5.83	0.045	14.53±5.67	12.8±5.67	3735[e]	.036*

*p<.05
a = t statistic reported, b = 2xc chi square reported, c = rx2 chi square reported, d = rx2 Fischers reported
e = Mann Whitney u distribution reported

Table 14. Neonatal Birth Characteristics After a Lifestyle Intervention

Characteristic	Lifestyle Intervention (n = 97)	Usual Care (n = 99)	Lifestyle Intervention (n = 68)	Usual Care (n = 61)	Test Statistic	*p*
Study Weight (g)	3229±526	3108±500	3280±421	3160 ±468	-1.465	.146
Study length (cm)	49.6±2.5	49.4±2.3	49.84±1.983	49.8±2.034	-.325	.746
PEAPOD	(n = 95)	(n = 96)	(n = 68)	(n = 61)		
PEAPOD age (days)	2.86±5.34	2.86±5.34	2.54 ±2.1	2.34±1.8	-.589	.557
FM (g)	360±173	324±157	329 ±155	329 ±155	-.806	.422
FFM (g)	2871±404	2786±405	2920±335	2830 ±383	-1.433	.151
QMR	(n = 82)	(n = 87)	(n = 68)	(n = 61)		
Total FM (g)	542±189	509±179	555±171	535± 164	-.676	.500
Total LM (g)	2327±325	2211±314	2360± 262	2260±293	-2.149	.034*
TBW (g)	2452±334	2342+/-320	2480 ± 282	2390 ± 308	-1.827	.070

FM: Fat Mass
FFM: Fat-Free Mass
QMR: Quantitative Magnetic Resonance
LM: Lean Mass
TBW: Total Body Water
*p<.05

Aim 1

Describe maternal diet quality measured by NOVA and controlled for weight and energy intake and compare to the HEI overall score.

The following sub-aim examined differences between NOVA category intakes at pre intervention (week 14) and post intervention (week 35) using an independent sample t test. The independent-samples t-test was used to determine if a difference existed between the means of two independent groups on a continuous dependent variable. More specifically, it helped determine whether the difference between the two randomized groups or time points was statistically significant. Violations of the applicable assumptions of normality were examined using graphical examinations of distribution and Q-Q plots, along with significant p values by

the Shapiro Wilk test for all NOVA categories for the two variables, percentages of energy intake (PEI) and percentages of food weight (PFW). The assumption of homogeneity of variance was also tested using Levene's test and results from those procedures are reported in the appendices.[124–129]

Research Aim 1a

Investigate the change from pre to post intervention for the LI group in ultra-processed food intake and unprocessed/minimally processed food intake measured by NOVA in the context of weight and energy intake compared to the UC group.

For these data, the investigator elected to report the means of each group as the relative values of NOVA category contributions to the diet in percentage of energy intake (PEI) in kilocalories and percentage of food weight (PFW). This information was determined as relevant due to the previously reported disparities in NOVA categories 1 and 4 foods for energy density and weight in the literature.[124–131]

Means for NOVA categories expressed as PEI are reported in kilocalories; means for NOVA categories expressed as PFW are reported in grams. For the entire sample of women at pre intervention (n = 157), the population had a mean PEI for category 1 unprocessed foods of 38.2% ± 16.53%; at post intervention (n = 157), mean PEI of category 1 unprocessed food intake was 40.98%± 16.81%. The population had a mean PEI for category 2 culinary ingredient foods at pre intervention (n = 157) of 5.12%±6.99%; at post intervention (n = 157), the mean PEI for category 2 culinary ingredient foods was 5.17%±5.68%. The population had a mean PEI for category 3 processed foods at Pre intervention (n = 157) of 10.47%±10.38%; at Post intervention (n = 157) at the mean PEI for category 3 processed food intake was 9.52%±9.17%. The population had a mean PEI for category 4 ultra-processed foods at Pre intervention of

46.12%±18.55%; at Post intervention (n = 157), the mean PEI for category 4 ultra-processed food was 44.33%±19.35%. Means for NOVA groups are expressed in percentage of food weight (PFW) in PFW. For the entire sample of women at Pre intervention (n = 157), the population had a mean percentage of food weight for category 1 unprocessed foods of 73.54 ± 16.85; at Post intervention (n = 157), the mean PFW for category 1 unprocessed foods was 75.86% ± 17.1%. The population had a mean PFW of category 2 culinary ingredient foods at Pre intervention (n = 157) of 0.83%±1.45%; at Post intervention (n = 157), the mean PFW of category 2 culinary ingredient foods was 0.75%±.93%. The population had a mean PFW of category 3 processed foods at Pre intervention (n = 157) of 3.16%±3.74%; at Post intervention (n = 157), the mean PFW category 3 processed foods was 2.73%±3.49%. The population had a mean PFW of category 4 ultra-processed foods of 22.47%±16.71%; at Post intervention (n = 157), the mean PFW category 4 ultra-processed foods was 20.65%±16.87% (see Table 15).

Table 15. Maternal Diet Description: Percentage of Kilocalories (PEI) and Percentage of Food Weight (PFW) Contributed by NOVA[1]

Recall	NOVA Category 1		NOVA Category 2		NOVA Category 3		NOVA Category 4		Absolute Totals	
	PEI	PFW	PEI	PFW	PEI	PFW	PEI	PFW	Kcals	Grams
Pre intervention (n=157)	38.3 ±16.5	73.5± 16.9	5.1±7	.83±1. 45	10.47± 10.38	3.16±3. 74	46.12 ±18.5 5	22.47±16 .71	1944 ±913.8	2973 ±104.6
Post intervention (n=157)	41±16. 8	75.9±17 .1	5.2±5.7	.75±.9 3	9.5±9. 2	2.7±3.5	44.3± 19.4	20.7±16. 9	1863 ±1018. 2	3178 ±132.9
Differences[a]	.1429	13583[b]	-.073	13100[b]	.865	11317[b]	.835	11304[b]	.739	13142[b]

[1] Category 1 = unprocessed, category 2 = processed culinary ingredients; category 3= processed; category 4 = ultra-processed

[a] Non-significant t statistics for category means

[b] Non-significant Mann Whitney U reported for category distributions

The investigator then compared the means for percentage of energy intake by NOVA categories 1 and 4, randomization assignment and time point using the independent t test. Boxplots were examined for significant outliers. PEI for category 1 foods for each group were normally distributed as determined by a Shapiro-Wilk's test (p > .05). There was homogeneity of

variances for categories 1 and 4 PEI for each group as determined by Levene's test (p = .811; p = .480). For the differences of unprocessed foods PEI within groups (see Table 16), a significant difference was detected between time points for the usual care group (t = -2.025, p = .045), but not for the intervention group for NOVA category 1 foods (t = -.003, p = .997). There were no significant differences across groups for PEI Category 1 (see Table 18).

Table 16. Differences *Within* Group Means in Category 1 Intake in Percentage of Energy Intake

	Pre intervention%	Post intervention%	t	df	Sig	Mean Difference	SE	Lower Bound	Upper Bound
Usual Care	36.32	42.02	-2.03	146	**.045***	-.057	.028	-.113	-.001
Lifestyle Intervention	40.04	40.05	-.003	164	.997	-.000	.025	-.05	.05

*p<.05

Table 17. Differences *Within* Group Means in Category 4 Intake in Percentage of Energy Intake

	Pre intervention%	Post intervention%	t	df	Sig	Mean Difference	SE	Lower Bound	Upper Bound
Usual Care	47.82	43.13	1.48	146	.141	.047	.032	-.016	.11
Lifestyle Intervention	44.6	45.4	-.277	164	.782	-.008	029	-.065	.049

The investigator repeated the independent t-test for the percentage of energy intake reported in category 4 foods. Boxplots were examined to determine if significant outliers were present in the data. PEI for category 4 foods for each group was normally distributed as determined by a Shapiro-Wilk's test (p > .05). There was homogeneity of variances for category 4 PEI for each group as determined by Levene's test (p = .426; p = .918). For the differences of ultra-processed food intake within groups (see Table 17), no significant difference was detected between pre intervention and post intervention for the usual care group's PEI for category 4 foods (t = 1.452, p = .149) and no significant difference was detected between pre intervention

and post intervention for the intervention group's PEI of category 4 foods (t = -.055, p = .956). No significant differences were detected for PEI category 4 foods across groups (see Table 19).

Table 18. Differences *Between* Group Means in Category 1 Intake in Percentage of Energy Intake

	Usual Care	Lifestyle Intervention	t	df	Sig	Mean Difference	SE	Lower Bound	Upper Bound
Pre intervention (%)	36.32	40.04	-1.41	155	.160	-.037	.026	-.089	.015
Post intervention (%)	42.02	40.05	.730	155	.466	.02	.027	-.335	.073

Table 19. Differences *Between* Group Means in Category 4 Intake in Percentage of Energy Intake

	Usual Care	Lifestyle Intervention	t	df	Sig	Mean Difference	SE	Lower Bound	Upper Bound
Pre intervention (%)	47.82	44.6	1.087	155	.279	.032	.03	-.026	.091
Post intervention (%)	43.13	45.4	-.732	155	.465	-.023	.031	-.084	.039

These analyses were repeated for percentage of PFW per NOVA group contributing to the diet. Boxplots were examined for significant outliers. Several outliers were reported by boxplot. Q-Q plots were examined for distribution and the outliers were identified via the scatterplot. A Shapiro-Wilk's test confirmed violation of assumption of normality with $p < .05$. The analysis was conducted using a Mann Whitney U test that compared the distribution of the data rather than the mean.[124–131]

As evidenced in the assumption tests, these data appeared to violate the assumption of normal distribution and outliers were noted by visible examination of the data. Rather than drop the outlier values, the investigator ran a nonparametric Mann Whitney U test as interpretation is robust to these violations of assumptions. This test was used to determine if there were

differences in percentage of diet in PFW between Pre intervention and Post intervention for each group. Distributions of the PFW NOVA category 1 for Pre intervention and Post intervention were similar as assessed by visual inspection for each randomization group. For differences within groups (see Table 20), distribution of NOVA category 1 score for the Usual Care group at Pre intervention (68.51%) and Post intervention (80.49%) were not significantly different (U = 3181, p = .089) and distribution of PFW for category 1 for the intervention group at Pre intervention (81.22%) and Post intervention (85.78%) was not statistically significantly different (U = 334, p = .541). No significant differences were detected between groups for PFW NOVA category 1 at either time point (see Table 22).

Table 20. Differences *Within* Group Distributions in Category 1 Intake in Percentage of Food Weight

	Pre intervention%	Post intervention%	N	MWU	SE	Sig
Usual Care	68.51	80.49	148	3181.00	260.8	.089
Lifestyle Intervention	81.22	85.78	166	3634.00	309.6	.541

Table 21. Differences *Within* Group Distributions in Category 4 Intake in Percentage of Food Weight

	Pre intervention%	Post intervention%	N	MWU	SE	Sig
Usual Care	78.76	70.24	148	2423	260.8	.227
Lifestyle Intervention	86.00	81.00	166	3237	309.6	.503

These analyses were repeated for PFW per NOVA category 4 contribution to the diet. Several outliers were reported by boxplot. Q-Q plots were examined for distribution and the outliers were visible via scatterplot. A /-Wilk's test confirmed violation of assumption of normality ($p < .05$). As evidenced in the assumption tests, these data appeared to violate the

assumption of normal distribution and outliers exist in the data. The investigator decided to run a nonparametric Mann Whitney U test to address these violations of assumptions. This test was used to determine if there were differences in percentage of diet in PFW NOVA category 4 between Pre intervention and Post intervention for each group. Distributions of the NOVA category 4 PFW for Pre intervention and Post intervention were similar as assessed by visual inspection for each randomization group. For differences within groups (see Table 21), distribution of the NOVA category 4 score for the Usual Care group at Pre intervention (78.76) and Post intervention (70.24) was not significantly different (U = 2423, p = .22) and distribution of NOVA category 4 PFW for the intervention group at Pre intervention (86) and Post intervention (81) was not statistically significantly different (U = 3237, p = 503). No significant differences were detected between groups for PFW NOVA category 4 at either time point (see Table 23).

Table 22. Differences *Between* Group Distributions in Category 1 Intake in Percentage of Food Weight

	Usual Care	Lifestyle Intervention	N	MWU	SE	Sig
Pre intervention	75.68	81.96	157	3317.00	284.376	.387
Post intervention	79.38	78.66	157	3043.00	284.376	.922

Table 23. Differences *Between* Group Distributions in Category 4 Intake in Percentage of Food Weight

	Usual Care	Lifestyle Intervention	N	Mann Whitney U	SE	Sig
Pre intervention	81.51	76.76	157	2885.00	284.376	.513
Post intervention	79.04	78.96	157	3068	284.376	.992

Research Aim 1b

Compare pre and post ultra-processed food shares of the diet changes to pre and post HEI overall scores in the context of weight of food.

This sub-aim used correlations. The Pearson product-moment correlation was used to determine the strength and direction of a linear relationship between two continuous variables. More specifically, the test generated a coefficient called the Pearson correlation coefficient, denoted as *r* (i.e., the italic lowercase letter r), and this coefficient measured the strength and direction of a linear relationship between two continuous variables. Its value can range from -1 for a perfect negative linear relationship to +1 for a perfect positive linear relationship. A value of 0 (zero) indicates no relationship between two variables. All variables here were measured on a continuous scale from 0 -100.[124–131]

First, data were examined for any violations of assumptions in PFW category 1 and category 4. For categories 1 and 4, a Shapiro-Wilk's test reported $p < .05$ for PFW at both timepoints. Outliers were visually assessed via boxplots and Q-Q plots. HEI overall scores at Pre intervention and at Post intervention did not violate this assumption. Thus, a Spearman's rank correlation was used to assess associations. One hundred and fifty-eight women were included in this analysis. NOVA category 1 PFW at Pre intervention was positively and weakly correlated with HEI at Pre intervention at the $p < .001$ level, and NOVA category 4 PFW at Pre intervention was negatively and moderately correlated with HEI at Pre intervention at the $p < .001$ level (see Table 24). Nor was category PFW at Post intervention correlated with HEI at Post intervention.

Research Aim 1c

Compare pre and post ultra-processed food shares of the diet to the pre and post HEI overall scores controlling for calorie intake:

First, data were examined for any violations of assumptions in PEI category 1 and category 4. Outliers were visually assessed via boxplots and Q-Q plots. Violations of normal distribution were not present in the PEI data, as demonstrated by a Shapiro-Wilk's test ($p > .05$). Only a few outliers existed in the kilocalorie data for recall 2, which was to be expected. Q-Q plots also confirmed these data satisfied the assumptions necessary to interpret the analysis.

A Pearson's product-moment correlation was run to assess the relationship between PEI of category 1 foods at Pre intervention and HEI at Pre intervention in a population of pregnant women with overweight or obesity. One hundred and fifty-eight women were included in this analysis. Preliminary analysis showed the relationship to be linear with both variables normally distributed as assessed by a Shapiro-Wilk's test ($p > .05$), and there were only two outliers. There was a statistically significant, weak positive correlation with category 1 food intake and HEI at Pre intervention, $r (157) = .321$, $p < .01$, and there was a statistically significant, moderate negative correlation with category 4 food intake and HEI at Pre intervention, $r (157) = -.433$, $p < .01$ (see Table 24). These correlations were not significant for category 1 and HEI at Post intervention, $r (157) = .059$. These correlations were not significant for category 4 foods and HEI at Post intervention, $r (157) = -.033$.

Correlations were also assessed for specific HEI components related to processing. These components changed between groups significantly at Post intervention for Whole Fruits ($p = .004$) and for Solid Fats, Alcohol and Added Sugar (SoFAAS) ($p = .036$). Due to non-normal distributions observed in these components, Spearman's rank correlation was used. Whole Fruits at Pre intervention had a statistically significant weak negative correlation with PEI category 4 intake at the $p < .05$ level, but no other correlations were observed (Table 25). None of these correlations were significant at Post intervention. SoFAAS had statistically significant

correlations with category 1 PFW and category 4 PFW and category 1 PEI and category 4 PEI at the p < .01 level at Pre intervention (Table 25). None of these correlations were observed at Post intervention.

Table 24. Correlations of Category 1 and 4 by NOVA with Overall Scores from the HEI Pre and Post Intervention

	HEI and Recall 1at Pre intervention	HEI and Recall 2 at Post intervention
Category 1 PFW[1]	.297**	.046
Category 4 PFW	-.319**	-.024
Category 1 PEI[2]	.321**	.059
Category 4 PEI	*-.433***	*-.033*

**p < .01
[1] Spearman's rank
[2] Pearson's correlation

Table 25. Correlations of Category 1 and 4 Food by NOVA with HEI Components Pre and Post Intervention

	HEIX04 Whole Fruits		HEIX12 SOFAAS	
	Pre intervention	Post intervention	Pre intervention	Post intervention
Category 1 PFW	.130	.644	.370**	.044
Category 4 PFW	-.140	.083	-.359**	-.022
Category 1 PEI	.120	-.009	.340**	.041
Category 4 PEI	-.163*	.121	-.277**	-.033

**p < .01, *p < .05
[1] Spearman's Rank
[2] Pearson Correlation

Aim 2

Investigate the relationship between gestational weight gain and diet quality as measured by NOVA.

A binomial logistic regression attempts to predict the probability that an observation falls into one of two categories of a dichotomous dependent variable based on one or more independent variables that can be either continuous or categorical. The investigator was not attempting to determine the predicted value of the dependent variable, but the probability of being in a particular category of the dependent variable given the independent variables. This model contains a dichotomous dependent variable represented at the population data level and at the IOM level. An excessive GWG (EGWG) was determined for this population by the descriptive statistic of mode. A second model included the IOM guidelines of 8.9kg maximum gestational weight gain for a pre-pregnancy BMI > 24.9; this was represented as EGWG_2. The covariates were explored in relationship to dependent variable EGWG and EGWG_2 to ensure no violations of assumptions. Observations were independent, capturing only food recalls at Post intervention. Linearity of the continuous variable with respect to the logit of the dependent variable was assessed via the Box-Tidwell procedure. A logit transformation of the dependent variable was also examined to assess linear relationships between continuous independent variable, PEI category 4, and the dependent variable. A Bonferonni correction was applied using all terms in the model resulting in statistical significance being accepted when $p < .0125$. The assumption of linearity held. Multicollinearity was explored and only one NOVA category, category 4 PEI, was used in the final model. Due to the homogeneous sample of college education and income, college education was excluded from the final model. Interactions between covariates and PEI 4 intake were explored (RACE and PEI 4; INCOME and PEI 4,

parity and PEI 4, and obesity and PEI 4). Interaction between obesity and PEI 4 intake was significant. Included in the final model were the categorical variables of race, obesity status, and the continuous variable of category 4 PEI on EGWG and EGWG_2.[124-132]

Research Aim 2a

Examine whether the independent variable, diet quality as measured by consumption of foods categorized by NOVA as ultra-processed, has an effect on the GWG experience for mothers in both LI and UC related to Post intervention intake of ultra-processed foods adjusted for weight of food and adjusted for total energy intake.

A binomial logistic regression was performed to ascertain the effects of obesity, race category 4 food intake, and the interaction of obesity and category 4 intake on the likelihood that participants gained excessive gestational weight. The logistic regression model was statistically significant ($x^2(156) = 41.166$, $p < .001$). The model met the Hosmer and Lemeshow test ($p > .05$). The model explained 31.4% (Nagelkerke R^2) of the variance in excessive gestational weight gain and correctly classified 74.4% of the cases. Sensitivity was 59.0%, specificity was 84.2%, positive predictive value was 76.2%, and negative predictive value was 70.6%. The area under the ROC curve was .764 (95% CI, .710–.818), an acceptable level of discrimination according to Hosmer et al. (2013). Of the four predictive variables, race, PEI Category 4, and the interaction of obesity and category 4 were significant, as shown in Table 26. Having obesity did not significantly add to the model ($p = .787$). For those who were non-white, the odds of gaining excessively increased by 2.5 than those who were white ($p = .023$). In addition, for everyone percentage point increase in ultra-processed food energy intake, the odds of gaining excessive gestational weight gain increased ($p = .014$). However, in the presence of the interaction term,

being with obesity and increased PEI 4 intake increased participants' odds of gaining excessively 91.5 times more than not being obese and having a lower PEI 4 intake.

Table 26. Summary of Logistic Regression Analysis of Excessive Gestational Weight Gain (EGWG = 7.4kg)

	B	SE	Wald	df	Sig	Exp (b)	95% C.I. for Exp(b) Lower	Upper
Race[a]	.916	.403	5.156	1	.023*	2.499	1.134	5.509
Obesity[b]	-.239	1.044	.052	1	.819	.787	.102	6.1
PEI Category 4	-4.731	1.917	6.091	1	.014*	.009	.000	.378
Obesity x PEI Category 4	4.517	2.273	3.950	1	.047*	91.598	1.064	7884.094
Constant	1.138	.841	1.832	1	.176	3.122		

Model Chi square=41.166
Nagelkerke R^2=31.4%
[a] Reference category = Caucasian
[b] Reference category = Overweight
*p<.05

For the second model, the dependent variable EGWG_2 was based on IOM guidelines for pre-pregnancy BMI > 24.9. A binomial logistic regression was performed to ascertain the effects of obesity, race, category 4 food intake, and the interaction of obesity and category 4 food intake on the likelihood that participants gained excessive gestational weight. The logistic regression model was statistically significant $x^2(156) = 24.487$, $p < .001$). The model explained 19.4% (Nagelkerke R^2) of the variance in excessive gestational weight gain and correctly classified 68.6% of the cases. Sensitivity was 69.4%, specificity was 67.9%, positive predictive value was 64.9%, and negative predictive value was 77.2%. The area under the ROC curve was .704 (95% CI, .647–.762), an acceptable level of discrimination according to Hosmer et al. (2013). The model met the Hosmer and Lemeshow test ($p > .05$). Of the four predictive variables, race and PEI category 4 were borderline predictors of excessive gestational weight gain ($p = .010$, OR = 2.492), as shown in Table 27.

Table 27. Summary of Logistic Regression Analysis of Excessive Gestational Weight Gain (EGWG = 9.8kg)

	B	SE	Wald	Df	Sig	Exp(b)	95% C.I For Exp(B)		R^2
							Upper	Lower	
Race[a]	.667	.363	3.383	1	.066	1.949	.957	3.969	
Obesity[b]	.438	.987	.197	1	.657	1.549	.224	10.712	
PEI Category 4	-3.529	1.888	3.494	1	.062	.029	.001	1.187	
Obesity x PEI Category 4	1.892	2.166	.763	1	.382	6.633	.095	462.705	
Constant	.283	.825	.118	1	.732	1.327			

Model Chi squared = 24.487
Nagelkerke R^2=19.4%
[a] Reference category = Caucasian
[b] Reference category= Overweight

Aim 3

Investigate the relationship between maternal diet quality as measured by NOVA and neonatal body composition and compare the results of the two anthropometric measures.

Research Aim 3a

Investigate an association between the group differences in maternal diet quality related to ultra-processed food intake as measured by NOVA and neonatal lean mass as measured by QMR.

A linear regression was run to investigate the effect of category 4 ultra-processed foods on neonatal lean mass as measured by QMR. To assess linearity, a scatterplot of PEI category 4 against lean mass was superimposed with a regression line. Visual inspection of these two plots indicated a linear relationship between variables. Outliers were identified and included in the analysis. A simple linear regression assessed the linear relationship between two continuous variables to predict the value of a dependent variable based on the value of an independent

variable. There was independence of residuals, as assessed by a Durbin Watson statistic of 1.7043 for Lifestyle Intervention and 2.043 for Usual Care. There was homoscedasticity, as assessed by visual inspection of a plot of standardized residuals versus standardized predicted values. Residuals were normally distributed as assessed by visual inspection of a normal probability plot.[124-133]

For the control group, the prediction model was significant F (4, 56) = 37.164, p < .001 with adjusted R^2 = 70.7 (see Table 28). Length was a significant predictor of neonatal lean mass, with every .1-centimeter increase in length predicting a 1-gram increase in neonatal lean mass (p < .001). Fat mass was a significant predictor for lean mass, with every .45 gram-increase predicting a 1-gram increase in lean mass (p = .004).

Table 28. Summary of Regression Analysis - Lean Mass as Measured by QMR in Usual Care Group

QMR Usual Care Group	T	Sig	ß	F	df	p	Adjusted R^2
Overall Model				37.164	56	**.001***	70.7
Length (cm)	8.610	**.0008***	.101				
Fat (g)	3.029	**.004***	.441				
Ultra-processed Food Intake (PEI 4)	1.184	.241	.123				
Solid Fats, Alcohol, and Added Sugar (HEI 12)	-.517	.607	-.002				

Dependent variable: Neonatal Lean Mass by QMR
*p<.05

For the intervention group, the prediction model was significant, F (4, 63) = 24.269, p < .001 with adjusted R^2 = 58.1% (see Table 29). Only length was a significant predictor for neonatal lean mass in this model for the lifestyle intervention group; each .1-centimeter increase in length predicted a 1-gram increase in lean mass (p < .001).

Table 29. Summary of Regression Analysis on Neonatal Lean Mass as Measured by QMR in Lifestyle Intervention Group

QMR Lifestyle Intervention Group	T	*p*	ß	*F*	*df*	*p*	Adjusted R^2
Overall Model				24.269	63	.001*	58.1%
Length (cm)	6.741	.000*	.097				.
Fat Mass (g)	.119	.906	.018				
Ultra-processed Food Intake (PEI 4)	1.876	.065	.213				
Solid Fats, Alcohol, and Added Sugar (HEI 12)	-.536	.594	-.002				

Dependent variable: Neonatal Lean Mass by QMR
*p<.05

Research Aim 3b

Investigate an association between the group differences in maternal diet quality as measured by NOVA quality related to ultra-processed food intake and neonatal fat-free mass as measured by PEAPOD.

A linear regression was run to assess the effect of category 4 ultra-processed foods on neonatal lean mass as measured by PEAPOD. To assess linearity, a scatterplot of category 4 versus lean mass and a superimposed regression line were plotted. There was homoscedasticity, as assessed by visual inspection of a plot of standardized residuals versus standardized predicted values. Residuals were normally distributed as assessed by visual inspection of a normal probability plot. The dependent variable was fat-free mass (FFMASSKG) with independent variables, including neonatal length, neonatal fat mass, NOVA category 4 food PEI, and solid fat, alcohol, and added sugar intake. There was independence of residuals as assessed by a Durbin Watson statistic of 2.089 for Lifestyle Intervention and 2.093 for Usual Care. For the

control group, the prediction model was significant F (4, 56) = 37.933, p < .001 with adjusted R^2 = 71.2 (see Table 30). Length was a significant predictor of neonatal lean mass with every .15-centimeter increase in length predicting a 1-gram increase in neonatal lean mass (p < .001).

Table 30. Linear Regression of Percentage of Energy Intake of Ultra-processed foods on Neonatal Fat-Free Mass as Measured by PEAPOD in Usual Care Group

PEAPOD Usual Care Group	*t*	*p*	ß	*F*	*df*	*p*	Adjusted R^2
Overall Model				*37.933*	*56*	*.001**	71.2
Length (cm)	10.702	.000*	.151				
Fat Mass (g)	1.651	.104	.310				
Ultra-processed Food Intake (PEI 4)	1.137	.260	.154				
Solid Fats, Alcohol and Added Sugar (HEI 12)	.691	.492	.003				

Dependent variable: Neonatal Fat Free Mass by PEAPOD
*p<.05

For the intervention group, the prediction model was significant, F (4, 63) = 24.463, p < .001 with adjusted R^2 = 60.3% (see Table 31). Length was a significant predictor for neonatal lean mass in this model for the lifestyle intervention group; each .13-centimeter increase in length predicted a 1-gram increase in lean mass (p < .001). In addition, ultra-processed food intake was also a significant predictor; for every.3% increase in this NOVA category, lean mass increased by 1 gram (p = .026)

Table 31. Linear Regression of Percentage of Energy Intake of Ultra-processed Foods on Neonatal Fat-Free Mass as Measured by PEAPOD in Lifestyle Intervention Group

PEAPOD Lifestyle Intervention Group	T	Sig	ß	*F*	*df*	*p*	Adjusted R^2
Overall Model				26.463	63	.001*	60.3%
Length (cm)	8.351	.000*	.132				
Fat Mass (g)	-1.280	.205	-.223				
Ultra-processed Food Intake (PEI 4)	2.275	.026*	.321				
Solid Fats, Alcohol, and Added Sugar (HEI 12)	-1.022	.311	-.005				

Dependent variable: Neonatal Fat Free Mass by PEAPOD
*p<.05

Additional analyses were run to assess relationships between PEI 4 and HEI 12 on neonatal lean tissue as measured by QMR and fat-free mass by air displacement plethsymography for the entire sample. All models met assumptions necessary to interpret results with Durbin Watson statistics above 2.

For the QMR method, the prediction model was significant, $F(4,124) = 55.250$, $p < .001$ with adjusted $R^2 = 62.9\%$ (see Table 32). Length was a significant predictor for neonatal lean mass in this model; each .1-centimeter increase in length predicted a 1-gram increase in lean mass ($p < .001$). Fat mass was also a significant predictor; every .23-gram increase predicted a 1-gram increase in lean mass. In addition, ultra-processed food intake was a significant predictor; for every .2%-increase in this NOVA category, lean mass increased by 1 gram ($p = .041$).

Table 32. Linear Regression of Percentage of Energy Intake of Ultra-Processed Foods on Neonatal Lean Mass as measured by Quantitative Magnetic Resonance

QMR	T	*p*	ß	*F*	*df*	*p*	Adjusted R^2
Overall Model				55.250	124	**.001***	62.9%
Length (cm)	10.673	**.000***	.099				
Fat Mass (g)	2.121	**.036***	.231				
Ultra-processed Food Intake (PEI 4)	2.070	**.041***	.164				
Solid Fats, Alcohol, and Added Sugar (HEI 12)	-.003	**.**998	-.000007				

Dependent variable: Neonatal Lean Mass by QMR
*p<.05

For the PEAPOD method, the prediction model was significant, F (4,124) = 58.622, $p < .001$ with adjusted $R^2 = 64.3\%$ (see Table 33). Length was a significant predictor for neonatal lean mass in this model for the lifestyle intervention group; each .14-centimeter increase in length predicted a 1-gram increase in lean mass ($p < .001$). In addition, ultra-processed food intake was also a significant predictor; for every .2%-increase in this NOVA category, lean mass increased by 1 gram ($p = .035$)

Table 33. Linear Regression of Percentage of Energy Intake of Ultra-processed Foods on Neonatal Fat-Free Mass as Measured by Air Displacement Plethsymography

PEAPOD	T	Sig	B	*F*	*df*	*p*	Adjusted R^2
Overall Model				58.622	124	**.001***	64.3
Length (cm)	13.364	**.000***	.143				
Fat Mass (g)	.076	.940	.010				
Ultra-processed Food Intake (PEI 4)	2.130	**.035***	.212				
Solid Fats, Alcohol and Added Sugar (HEI 12)	.184	.854	.001				

Dependent variable: Neonatal Fat Free Mass by PEAPOD
*p<.05

Chapter 5

DISCUSSION

The main aim of this study was to investigate the usefulness of the NOVA guidelines for assessing diet quality in a cohort of pregnant women with overweight or obesity and its relationships to their own anthropometric outcomes and to the body composition outcomes in their offspring. The optimal method of nutrition intervention and education for this special population remains unknown; using NOVA may provide health care professionals with a different lens to assess diet quality and nutrition educators with additional vocabulary to convey more tailored messages regarding optimal nutrition strategies for mother and offspring.

The HEI and even other systems for judging diet quality that are food-based such as the Food Quality Score[135] do not take into account degree of processing of the foods. At the same time, there are systems for classifying foods based on processing. Many of these categorize the many processed foods in the current food system in order to serve regulatory purposes. These systems do not take into account the healthfulness of the food, noting that there are both more healthful and less healthful foods in each of the processed foods categories[53] and many processed foods are fortified as a method to improve or maintain adequate intakes of nutrients of the American diet via enrichment or fortification.

Many would say the HEI is sufficient a measure of diet quality. However, the NOVA guidelines allow researchers to look at another characteristic of food consumption that is more holistic: degree of processing. Fardet emphasizes this point by stating that the health potential of food does not result from chemical composition alone and that the nutrient interactions along with the physical structure of the food can affect satiation, gut motility, nutrient bioavailability, inflammation or metabolic syndrome.[93] While the HEI is based on nutrients and a few specific

food categories, NOVA takes a different look at how structure of food is also related to important effects apart from adequate nutrient intake such as appetitive behavior and physiological responses.

In particular, the NOVA guidelines place an emphasis on ultra-processed foods, which have recently become a larger percentage of the diet in high- and middle-income countries and seem to be increasing in lower income countries as well.[45, 46, 52] There has been expressed concern that these food items are displacing more traditional dishes and unprocessed food selections.[91] Within the last decade, many studies have looked cross-sectionally and longitudinally at the increased intake of ultra-processed foods and how that may impact human health within the context of rising rates of obesity, metabolic syndrome and other non-communicable diseases.[43-46, 94-97] NOVA has allowed for this body of literature to amass as it clearly and specifically defines ultra-processed food as:

"formulated mostly or entirely from substances derived from foods, typically contain little or no whole foods" and specifies its ingredients as "not available from retail outlets…numerically the majority of ingredients are preservatives; stabilizers, emulsifiers, solvents, binders, bulkers; sweeteners, sensory enhancers, colors and flavors; processing aids and additives. Processes include hydrogenation, hydrolysis, extruding, molding, reshaping; pre-processing by frying, baking." [48]

This clear definition provides a new lens to look through when analyzing associations of foods with human health and is much different from other food processing classification systems as it addresses food in a more comprehensive manner.

This study was conducted in that context to see whether the NOVA guidelines approach would provide additional information to HEI regarding diet quality of women during pregnancy

and the consequent impact on maternal gestational weight gain and neonatal body composition outcomes.

In terms of maternal outcomes, one major finding of this study was that there were significant correlations between the Healthy Eating Index (HEI) and the NOVA guidelines for the data obtained at baseline before the start of the intervention (pre intervention). The intake of unprocessed foods measured both as a percentage of energy in the diet and as a percentage of food weight in the diet *positively* correlated with HEI scores for the sample at the beginning of the study. In addition, the intake of ultra-processed food, also measured both as a percentage of energy in the diet and as a percentage of food weight in the diet, was *negatively* correlated with HEI scores. These significant correlations suggest that both NOVA and the HEI are measuring diet quality in similar fashion for the sample at the beginning of the study. Rohatgi et al[40] obtained similar findings in a study comparing percentage of energy intake of ultra-processed foods to the HEI. They did not examine the relationship of unprocessed food to the HEI or the associations in terms of food weight. To the investigator's knowledge, this is the first study to directly compare the NOVA to HEI systems for both unprocessed and ultra-processed food. However, at the end of the study these correlations did not hold.

In addition to significant correlations with HEI overall scores, there were also significant correlations of the NOVA scores with the HEI 12 Solid fats, alcohol and added sugar (SOFAAS) score at baseline. SOFAAS decreased between groups from Pre intervention to Post intervention ($p=.036$). As was observed with the overall HEI score, these correlations that were present at baseline, again did not hold at the end of the study.

This is puzzling. One of the explanations for why the correlations did not hold at post intervention could be related to the quality of the dietary data itself. For the parent study and the

current study, only one 24-hour recall was collected at each time point per mother pre and post intervention. While this is sufficient when comparing group means in large datasets [135] it may provide only a snap shot of mothers' food intake for one day when used in analyses based on individual person data. While the ASA24 does ask the participant if the record was of the *intake* of a typical day, each individual report may not have been an accurate representation of a typical dietary *pattern*. The data showed that there were large standard deviations in total daily energy intake expressed in calories, suggesting instability of the data. Thus, it may be that the correlations found at pre intervention were chance findings. Clearly, these inconsistencies call for further research on the relationship between HEI and NOVA as measures of diet quality for this population.

An important objective of this study was to examine whether higher maternal diet quality measured using NOVA (fewer category 4 foods) would be associated with a lower degree of excessive gestational weight gain. The parent study had found that the intervention was able to successfully improve diet quality as measured by HIE and also to mitigate excessive gestational weight gain led. However, it found no significant statistical association between improved diet quality as measured by HEI with the attenuation in weight gain. In the current study, a main effect of ultra-processed food intake was significant for predicting excessive gestational weight gain (p=.014), but in an unexpected direction when based on the study participants parameters (decreased use of ultra-processed food was associated with excessive weight gain), while it was borderline significant (p=.062) in the hypothesized direction based on IOM guidelines for weight gain (increased use of ultra-processed food was associated with excessive weight gain).

In addition, while the main effect of having obesity was not a significant predictor of gestational weight gain, the interaction effect of having obesity and having an increased ultra-

processed food intake was significant and in an expected direction. That is, for those who had obesity, a higher intake of ultra-processed food was predictive of excessive weight gain. These conflicting findings likely result from the instability of the dietary data. This interpretation seems to be borne out by the fact that a similar study did obtain clear results in the hypothesized direction.[40] That study had a sample size of only 45. However, the dietary data were based on a food frequency questionnaire which asked about intake in the month prior, and thus provided more stable dietary intake data. The sample was also more representative of the national pattern in terms of the intake of NOVA food categories.

This suggests that the conflicting results may also be associated in part with the nature of the diets of participants in the current study. Their diet quality as measured by NOVA at baseline was not typical of the American intake as measured by NOVA: these women were eating much more healthfully. For this population, the largest distributions of food intake in terms of the NOVA categories were found in category 1, unprocessed/ minimally foods, and category 4, ultra-processed foods which is similar to what has been demonstrated in other studies of other populations. However, the percentage of energy intake from category 1 at pre intervention and post intervention were higher, and the percentage of energy intake from category 4 at pre intervention and post intervention were lower than the national average found in previous publications on US national data that used the same technique for categorization. [52] For example, the category 1 intake of unprocessed/ minimally foods at pre intervention and post intervention for this study's population was 38.3 and 41% respectively; the national average for the Unites States is 30.2%.[52] For ultra-processed foods, this sample's intakes at pre intervention and post intervention were 46.1 and 44.3% respectively; the national average for the United States is 57.5%.[52] In terms of total energy intake, the national average as reported in the

Martinez-Steele analysis of NHANES data in 2017 was 2069.9 kcal/day[52]; pre intervention and post intervention for this population were 1943.5 and 1863 kcal/day, respectively. The LIFT intervention empathized reducing fat and calories in the diet to prevent excessive weight gain. It may be speculated that the women were able to maintain their calorie intake and attenuate excessive weight gain because of judicious use of ultra-processed low fat and low-calorie substitutes for contributing to the inconsistent results in the study. Anecdotally, it was seen that there were many entries for low-calorie but ultra-processed foods in the dietary records. Clearly, this is an area requiring further investigation

A main effect of was found for race, with being non-white, increased the odds of gaining excessive gestational weight by a factor of 2.5. This is in agreement with the literature [137]. It must also be noted that this was a homogenous sample with regard to socioeconomic status (65% making more than $75,000/year) and education (75% having college degrees) and with 45% of the sample size being white. With a larger sample and increased variability in the sample, this finding may not hold as the beta weight was small (.916).

In terms of neonatal outcomes, findings from this study suggest that length and fat mass are significant predictors of lean mass in neonates.[138] This is in line with the literature. In terms of the relationship with maternal diet, there was a significant association between maternal ultra-processed food intake and neonatal lean mass; that is, the higher the consumption of ultra-processed food, the greater the neonatal lean mass This was not in the hypothesized direction. For the model run using the entire population for each body composition method (QMR and PEAPOD), ultra-processed food significantly predicted lean mass where SOFAAS did not. While being significant, however, the association was minimal with very small beta weights. Moreover, when plotting the regression line, it is quite flat and is thus is probably not clinically

meaningful. This finding is somewhat similar to that from parent study, which did not find an association between observed improved HEI scores and increased neonatal lean mass in the intervention group.

It may be that including a larger number of participants with a diet more representative of the national average diet quality as measured by NOVA may have changed the slope of the regression line and provided more meaningful data. However, these findings could also be related to the tenuous one day recall data and be chance findings.

Limitations of the Study

While the study sample was larger than previously published data on a similar population[40], the sample size was still relatively small. In addition, in the recent publication, a food frequency questionnaire (FFQ) was used. While this was cited as a limitation in their study, the current study suggests that 24-hour dietary recalls may not be the answer and indeed was a limitation. An average of three 24-hour recalls would have provided more consistent data and perhaps more conclusive evidence. The small sample size makes it difficult to draw strong conclusions; with a larger sample size the group means of the singular ASA24 recalls could have been analyzed in a more meaningful way.[136] In addition, the sample size had limited variability due to its homogenous characteristics of the mothers at pre-intervention.

As the NOVA food classification was applied posteriori from the entry and coding of the recalls, it is possible that some foods were misclassified. However, the methods used to categorize foods according to NOVA has been used in other publications.[52, 95, 101, 102] In addition, other studies have taken a more detailed approach and incorporated specific nutrients into their models. For example, Martinez Steele[52], Rohatgi[40], Batal[97] and Hall[139] assessed nutrients such as protein, fiber, sugar and salt and this may have been able to provide more description regarding

differences between groups. However, the intent of the study was to approach diet quality from a more holistic perspective.

There is always an inherent bias with field collected and self-reported dietary intake data.[140.] In addition, the intervention which taught portion control and food logging skills may have made a difference in the reported post-intervention intakes in terms of the NOVA categories. In addition, there were certain data that were not available to the researcher that may have also contributed to the study outcomes, such as physical activity, sleep quality, stress levels, pre-pregnancy BMI and other factors that affect energy balance and satiety. This study can serve as an exploratory study for understanding the impact of maternal diet quality as measured by NOVA on gestational weight gain and neonatal body composition. Further research should use a larger and more diverse sample,-check data collection for confounders and include multiple recalls at each time point of data collection

Strengths of the Study

The parent study was a rigorously conducted randomized controlled trial and included strict inclusion criteria for screening and randomization. In addition, HEI and NOVA variables were analyzed using the exact same FNDDS food codes and SR code data. This is also the first study to examine the relationship of maternal intake of NOVA-defined ultra-processed foods to neonatal lean mass using QMR. Previous studies involving the NOVA guidelines have used food frequencies, engendering the criticism that the NOVA system cannot be applied to nutrient-specific datasets or used in more advanced analyses. This criticism thus seems unfounded

Implications for Practice and Research

Implications for Practice

Although the IOM and other public health and scientific communities have widely disseminated gestational weight gain recommendations for women with pre-pregnancy overweight or obesity, some 55% of women with pre-pregnancy normal weight and 65% of women with overweight/obesity continue to gain in excess of these guidelines.[2, 6, 56, 57] The results of the parent study suggest that women with overweight or obesity were able to gain within the recommendations as a result of the intervention. The results of the current study suggest that perhaps the use of ultra-processed foods in the context of healthy diet high in unprocessed/ minimally foods had little effect on gestational weight gain or neonatal outcomes, except among those with obesity, where increased use of ultra-processed food was associated with excess gestational weight gain. Therefore, healthcare providers should take advantage of prenatal visits as a window of opportunity to encourage unprocessed and minimally foods and help women make informed decisions regarding ultra-processed foods.

A recent study by Tseng et al[104] noted there is considerable "consumer confusion" that leads to "flawed substitutive behavior". They compared published MyPlate menus from USDA with the same menus based on commonly used ultra-processed foods and found that MyPlate meals made with ultra-processed foods cost 20% more and though they had fewer calories, they were higher in sugar and salt than meals with supermarket purchased minimally processed, whole foods. The authors conclude that thus "distinguishing ultra-processed from less processed foods may help consumers make healthier choices when using MyPlate tools, particularly in a food environment that presents a wide range of alternatives." [104] Nutrition professionals who become familiar with qualities of ultra-processed foods and their effects on satiation and

physiology may thus be able to provide more tailored guidance for patients and clients on how to make trade-offs with convenience and preparation time in a manner that also holistically addresses our current food environment.

Implications for Research

It remains important to know whether maternal ultra-processed food intake influences gestational weight gain and the body composition of the neonate. Given that this study was pilot in nature and had inconclusive results, future research should include utilizing similar data analyses on a population with a more nationally representative diet, a larger sample size, and a more robust measure of dietary intake such as three 24-hour recalls. A recent publication by Hall, et al[139] compared an ad libitum intake of unprocessed category 1 diet to an ad libitum intake of ultra-processed category 4 diet in a repeated measures design in the first randomized controlled trial to investigate causal effects between ultra-processed food consumption and obesity. This study did find a significant albeit small difference between diets related to energy intake, with increased energy intakes during the ultra-processed diet phase of the study. Certainly, further investigation to identify mechanisms and how this may affect fetal programming is warranted. Furthermore, it would be useful to identify qualities unique to specific ultra-processed foods[141], whether in the physical structure of the food item or the impacts on gut biome or other mechanisms, that may impact the health of women during pregnancy. It will be important for dietary intake assessment tools to provide probes that will help identify the level of processing for the food items consumed.

Conclusion

In conclusion, food processing has become a much more important aspect of dietary patterns and dietary quality in terms of its impact on body weight diet related diseases, health and well-being than was ever the case 20 or 30 years ago.[50] This study examined whether NOVA, a system for categorizing food by level of processing, is a better way to measure diet quality than the HEI for examining maternal and neonate anthropometry and body composition outcomes. The results were inconclusive. The consumption of ultra-processed foods was not related in any clinically meaningful to maternal excessive weight gain or neonatal lean body mass. These findings were likely because of dietary intake measurement issues and because the study participants were already eating a healthy diet. Including some ultra-processed foods did not seem to be detrimental. Further studies need to be conducted with a larger sample size using a more robust measure of dietary intake and with a population that is more representative of the nation as a whole. Given that a recent similar study found ultra-processed food to be highly predictive of maternal and neonatal outcomes, and many other studies have demonstrated that ultra-processed food is related to several health conditions in many countries that this study did not measure, it seems prudent for healthcare providers to take advantage of prenatal visits as a window of opportunity to encourage the consumption of unprocessed and minimally foods and help women make informed decisions regarding ultra-processed foods.

REFERENCES

1. Xavier Pi-Sunyer (2009) The Medical Risks of Obesity, Postgraduate Medicine, 121:6, 21-33, DOI: 10.3810/pgm.2009.11.2074

2. Tanentsapf I, Heitmann BL, Adegboye AR. Systematic review of clinical trials on dietary interventions to prevent excessive weight gain during pregnancy among normal weight, overweight and obese women. BMC Pregnancy Childbirth. 2011;11:81.

3. Lenoir-Wijnkoop, I, van der Beek, EM, Garssen, J. Health economic modeling to assess short-term costs of maternal overweight, gestational diabetes, and related macrosomia—a pilot evaluation. Frontiers in Pharmacology, 2015;6;103. doi:10.3389/fphar.2015.00103.

4. Institute of Medicine. Weight Gain During Pregnancy: Reexamining the Guidelines. Washington, DC: The National Academies Press; 2009.

5. Siega-Riz AM, Deierlein A, Stuebe A. Implementation of the new Institute of Medicine gestational weight gain guidelines. J Midwifery Women's Health. 2010;55:512-519. 10.1016/j.jmwh.2010.04.001.

6. Mercado A, Marquez B, Abrams B, Phipps MG, Wing RR, Phelan S. Where do women get advice about weight, eating, and physical activity during pregnancy? J Women's Health. 2017;26:9, 951-995.

7. Sharp GC, Lawlor DA, Richmond RC, Fraser A, Simpkin A, Suderman M, Shihab HA, Lyttleton O, McArdle W, Ring SM, Gaunt TR, Smith GD, Relton CL. Maternal pre-pregnancy BMI and gestational weight gain, offspring DNA methylation and later offspring adiposity: findings from the Avon Longitudinal Study of Parents and Children. Int J Epidemiol. 2015;44(4):1288-1304. https://doiorg.ezproxy.cul.columbia.edu/10.1093/ije/dyv042

8. Polley BA, Wing RR, Sims CJ. Randomized controlled trial to prevent excessive weight gain in pregnant women. Int J Obes Relat Metab Disord. 2002;26:1494-1502. 10.1038/sj.ijo.0802130.

9. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P. Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis. BMC Medicine. 2012;10:47.

10. Phelan S. Reducing excessive gestational weight gain: lessons from the weight control literature and avenues for future research. Women's Health. 2011;7(6):641-661.

11. Ramachenderan J, Bradford J, McLean M. Maternal obesity and pregnancy complications: a review. Aust N Z J Obstet Gynaecol. 2008;48:228-235. 10.1111/j.1479-828X.2008.00860.x.

12. Durnin JV. Energy requirements of pregnancy. Acta Pædiatrica. 1991;80:33-42.

13. Buschur E, Kim, C. Guidelines and interventions for obesity during pregnancy. Int J Gynaecol Obstet. 2012;119:6-10. doi:10.1016/j.ijgo.2012.04.025.

14. Clark M, Ogden J. The impact of pregnancy on eating behaviour and aspects of weight concern. Int J Obes Relat Metab Disord. 1999;23:18-24. 10.1038/sj.ijo.0800747.

15. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. *PLoS One*. 2013;8(4).

16. Boney C, Verma A, Tucker R. Metabolic syndrome in childhood: association with birth weight, maternal obesity and gestational diabetes mellitus. Pediatrics. 2005;15:3. doi:10.1542/peds.2004-1808.

17. Clifton R, Evans M, Cahill A, et al. Design of lifestyle intervention trials to prevent excessive gestational weight gain in women with overweight or obesity. Obesity. 2016; 24:305-313. doi:10.1002/oby.21330.

18. Seward M, Simon D, Richardson M. Supporting healthful lifestyles during pregnancy: a health coach intervention pilot study. BMC Pregnancy Childbirth. 2018;18:375. doi:10.1186/s212884-018-2010-z.

19. Dodd JM, Crowther CA, Robinson JS. Dietary and lifestyle interventions to limit weight gain during pregnancy for obese or overweight women: a systematic review. Acta Obstet Gynecol Scand. 2008;87:702-706. 10.1080/00016340802061111.

20. Asbee SM, Jenkins TR, Butler JR. Preventing excessive weight gain during pregnancy through dietary and lifestyle counseling: a randomized controlled trial. Obstrec Gynecol 2009;113.

21. Polley BA, Wing RR, Sims CJ. Randomized controlled trial to prevent excessive weight gain in pregnant women. Int J Obes Relat Metab Disord. 2002;26:1494-1502.

22. Gallagher D, Rosenn B, Toro□Ramos T, Paley C, Gidwani S, Horowitz M, Crane J, Lin S, Thornton JC, Pi□Sunyer X. Greater neonatal fat-free mass and similar fat mass following a randomized trial to control excess gestational weight gain. Obesity. 2018;26:578-587.

23. Vesco KK, Karanja N, King JC, et al. Efficacy of a group-based dietary intervention for limiting gestational weight gain among obese women: a randomized controlled trial. Obesity. 2014;22:1989-1996.

24. Norman JE, Reynolds R. The consequences of obesity and excess weight gain in pregnancy. Proc Nutr Soc. 2011;70(4):450-456.

25. Almond D, Currie J. Killing me softly: the fetal origins hypothesis. J Econ Perspect. 2001;25(3):153-172. doi:10.1257/jep.25.3.153.

26. Brenseke B, Prater MR, Bahamonde J, Gutierrez JC. Current thoughts on maternal nutrition and fetal programming of the metabolic syndrome. J Pregnancy 2013:368461. http://dx.doi.org.10.1155.2013/368461.

27. Barker D. Developmental origins of chronic disease. Public Health. 2012;126(3):185-189.

28. Friis C, Qvigstad E, Roland M, et al. Newborn body fat: associations with maternal metabolic state and placental size. PLos ONE. 2013;8(2):e57467. doi:10.1371/journal.pone.0057467

29. Godfrey KM, Sheppard A, Gluckman PD, Lillycrop KA, Burdge GC, McLean C et al. Epigenetic gene promoter methylation at birth is associated with child's later adiposity. Diabetes. 2011;60(5):1528-1534.

30. Goodspeed D, Seferovic MD, Holland W, Mcknight RA, Summers SA, Branch DW et al. Essential nutrient supplementation prevents heritable metabolic disease in multigenerational intrauterine growth-restricted rats. FASEB J. 2015;29(3):807-819.

31. Lorite Mingot D, Gesteiro E, Bastida S, Sánchez-Muniz FJ. Epigenetic effects of the pregnancy Mediterranean diet adherence on the offspring metabolic syndrome markers. J Physiol Biochem. 2017;73:495. https://doi-org.ezproxy.cul.columbia.edu/10.1007/s13105-017-0592-y

32. Gesteiro E, Bernal BR, Bastida S, Sánchez-Muniz FJ. Maternal diets with low healthy eating index or Mediterranean diet adherence scores are associated with high cord-blood insulin levels and insulin resistance markers at birth. Eur J Clin Nutr. 2012;66(9):1008-1015.

33. Metzger B, Lowe L, Dyer A, et al. Hyperglycemia and adverse pregnancy outcome study: associations with neonatal anthropometry. Diabetes. 2009;58(2).

34. Horan M, McGowan C, Gibney E, et al. Maternal low glycemic index diet, fat intake and postprandial glucose influences neonatal adiposity—secondary analysis from the ROLO study. Nutr J. 2014;13:78. doi:10.1186/1475-2891-13-78.

35. Shapiro ALB, Ringham BM, Glueck DH, Norris JM, Barbour LA, Friedman JE, Dabelea D. Infant adiposity is independently associated with a maternal high fat diet but not related to niacin intake: the Healthy Start Study. Matern Child Health J. 2017;21(8):1662-1668. doi:10.1007/s10995-016-2258-8.

36. Shapiro AL, Kaar JL, Crume TL, Starling AP, Siega-Riz AM, Ringham BM, Glueck DH, Norris JM, Barbour LA, Friedman JE, Dabelea D. Maternal diet quality in pregnancy and neonatal adiposity: the Healthy Start study. Int J Obesity. 2016;40:1056-1062. doi:10.1038/ijo.2016.79.

37. Kizirian N, Markovic T, Muirhead R, et al. Macronutrient balance and dietary glycemic index in pregnancy predict neonatal body composition. Nutrients. 2016;8(5):270.

38. Horan M, McGowan C, Gibney E, et al. The association between maternal dietary micronutrient intake and neonatal anthropometry—secondary analysis from the ROLO study. Nutr J. 2015;14:105. doi:10.1186/s12937-015-0095-z.

39. Ai-Ru C, de Seymour JV, Colega M, Chen L, Chan Y, Aris IM, Tint M, Quah PL, Godfrey KM, Yap F, Saw S, Baker PN, Chong Y, van Dam RM, Lee YS, Chong MF. A vegetable, fruit, and white rice dietary pattern during pregnancy is associated with a lower risk of preterm birth and larger birth size in a multiethnic Asian cohort: the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort study. Am J Clin Nutr. 2016; 104(5):1416-1423. https://doi.org/10.3945/ajcn.116.133892

40. Rohatgi KW, Tinius RA, Cade WT, Steele EM, Cahill AG, Parra DC. Relationships between consumption of ultra-processed foods, gestational weight gain and neonatal outcomes in a sample of US pregnant women. Peer J. 2017;5:e4091.

41. Millen BE, Abrams S, Adams-Campbell L, et al. The 2015 Dietary Guidelines Advisory Committee Scientific Report: Development and Major Conclusions. *Adv Nutr*. 2016;7(3):438–444. Published 2016 May 9. doi:10.3945/an.116.012120

42. Guenther P, Kirkpatrick S, Reedy J, et al. The healthy eating index-2010 is a valid and reliable measure of diet quality according to the 2010 dietary guidelines for Americans. J. Nutr 2014. 144; 399-407. Doi: 10.3945/jn/113.183079

43. Moubarac JC, Martins APB, Claro RM, Levy RB, Cannon G, Monteiro C. Consumption of ultra-processed food and likely impact on human health: evidence from Canada. Public Health Nutr. 2012. doi:10.1017/s1368980012005009.

44. Rauber F, Campagnolo P, Hoffman D, Vitolo, M. Consumption of ultra-processed food products and its effects on children's lipid profiles. Nutr Metab Cardiovasc Dis. 2015;25:116-122. doi:10.1016/j.numecd.2014.08.001.

45. Medonca R, Pimenta A, Gea A, et al. Ultraprocessed food consumption and risk of overweight and obesity: the University of Navarra follow-up (SUN) cohort study. Am J Clin Nutr. 2016;104:1433-1440.

46. Tavares LF, Costa Fonseca S, et al. Relationship between ultra-processed foods and metabolic syndrome in adolescents from a Brazilian Family Doctor Program. Public Health Nutrition. 2011;15:1

47. Fardet A, Rock E, Bassama J, et al. Current food classifications in epidemiological studies do not enable solid nutritional recommendations for preventing diet-related chronic diseases: the impact of food processing. Adv Nutr. 2015;6:629-638. doi:10.3945/an.115. 008789.

48. Monteiro C, Levy RB, Claro RM, de Castro IRR, Cannon G. A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica. 2010;26(11):2039-2049.

49. Monteiro C, Cannon G, Levy RB, Claro RM, Moubarac JC. Ultra-processing and a new classification of foods. In Neff R, ed. Introduction to U.S. Food System: Public Health, Environment and Equity. San Francisco, CA: Jossey Bass; 2015:338-339.

50. Moubarac JC, Parra D, Cannon G, Monteiro C. Food classification systems based on food processing: significance and implications for policies and actions: a systematic literature review and assessment. Curr Obes Resp, 2014. doi:10.1007/s13679-014-0092-0.

51. Poti J, Braga B, Qin B. Ultra-processed food intake and obesity: what really matters for health—processing or nutrient content? Curr Obes Rep. 2017;6:420-431. doi:10.1007/ s13679-017-0285-4.

52. Steele E, Popkin B, Swinburn B, Monteiro C. The share of ultra-processed foods and the overall nutritional quality of diets in the US: evidence from a nationally representative cross-sectional study. Popul Health Metr 2017;15:6. doi:10.1186/s12963-017-0119-3.

53. Jones JM. Food processing: criteria for dietary guidance and public health? *Proceedings of the Nutrition Society*. 2019;78(1):4-18. doi:10.1017/S0029665118002513

54. Gibney M, Forde C, Mullaly D, Gibney E. Ultra-processed food in human health: a critical appraisal. Am J Clin Nutr. 2017;107:717-724.

55. Spark A. Nutrition in Public Health: Principles, Policies, and Practice, Second Edition, Boca Raton, Florida. CRC Press, 2015

56. Herring SJ, Cruice JF, Bennett GG, Rose MZ, Davey A, Foster GD. Preventing excessive gestational weight gain among African American women: a randomized clinical trial. Obesity. 2016;24:30-36. doi:10.1002/oby.21240

57. Phelan S, Wing R, Brannen A, McHugh A, Hagobian T et al. Randomized controlled clinical trial of behavioral lifestyle intervention with partial meal replacement to reduce excessive gestational weight gain. Am J Clin Nutr. 2018; 107:183-194

58. Gardner B, Wardle J, Poston L, Croker H. Changing diet and physical activity to reduce gestational weigh tgain: a meta-analysis. Obesity Reviews. 2011; 12, e602-620.

59. Nelson S, Matthews P, Poston L. Maternal metabolism and obesity: modifiable determinants of pregnancy outcomes. Human Reproduction Update. 2009; 16:3, 255-275.

60. Lau E, Liu J, Archer E, McDonald S, Liu J. Maternal weight gain in pregnancy and risk of obesity among offspring: a systematic review. Journal of Obesity, Volume 2014.

61. Castro L, Avina R. 2002. Maternal obesity and pregnancy outcomes. Curr Opin obstet Gynecol 14: 601-606.

62. Mitanchez D, Chavatte-Palmer P. Review shows that maternal obesity induces serious adverse neonatal effects and is associated with childhood obesity in their offspring. Acta Paediatrica. 2018; 107, 1156-1165

63. Peaceman A, Clifton R, Phelan S, Gallagher D, Evans M, Redman L, Knowler W, et al. Lifestyle interventions limit gestational weight gain in women with overweight or obesity: LIFE-Moms prospective meta-analysis. Obesity, 2018; 26. 1396-1404

64. Dodd JM, Deussen AR, Mohamad I, Rifas-Shiman SL, Yelland LN, Louise J, McPhee AJ, Grivell RM, Owens JA, Gillman MW, Robinson JS. The effect of antenatal lifestyle advice for women who are overweight or obese on secondary measures of neonatal body composition: the LIMIT randomised trial. BJOG. 2016;123:244-253.

65. Grivell RM, Yelland LN, Deussen A, Crowther CA, Dodd JM. Antenatal dietary and lifestyle advice for women who are overweight or obese and the effect on fetal growth and adiposity: the LIMIT randomised trial. BJOG. 2016;123:233-243.

66. Tussing-Humphreys LM, Thomson JL, Goodman MH, Olender S. Maternal diet quality and nutrient intake in the gestational period: results from the delta healthy sprouts comparative impact trial. Matern Health, Neonatol Perinatol. 2016;2:8.

67. Olson C, von Kries, R. Interventions during pregnancy reduce excessive gestational weight gain but yield unexpected results on neonatal body composition. Obesity. 2017; 26:3.

68. Langford A, Joshu C, Chang J. Does gestational weight gain affect the risk of adverse maternal and infant outcomes in overweight women? Matern Child Health J. 2011; 15: 860-865

69. Catalano PM, Thomas A, Huston-Presley L, Amini S. Increased fetal adiposity: a very sensitive marker of abnormal in utero development. Am J Obstet Gynecol. 2003; 189 1698-704.

70. Grandy M, Snowden JM, Boone-Heinonen J, Purnell JQ, Thornburg KL, Marshall NE. Poorer maternal diety quality and increased birth weight. The Journal of Maternal-Fetal and Neonatal Medicine. 2018; 31:12 1613-16-19

71. Andres A, Hull H, Shankar K, Casey P, Cleves M, Badger T. Longitudinal body composition of children born to mothers with normal weight, oberweight and obesity. Obesity. 2015; 23.

72. Papazian T, Tayeh GA, Sibai D, Hout H, Melki I, Rabbaa Khabbaz L. Impact of maternal body mass index and gestational weight gain on neonatal outcomes among healthy Middle-Eastern females. PLoS ONE. 2017; 12: 7.

73. Starling A, Suader KA, Kaar JL, Shapiro ALB, Siega-Riz AM. Maternal dietary patterns during pregnancy are associated with newborn body composition. J Nutr 2017;147:1334-9.

74. Mitanchez D, Jacquemint S, Nizard J, Tanguy M, Ciangura C, et al. Effect of maternal obesity on birthweight and neonatal fat mass: a prospective clinical trial. PLoS ONE. 2017; 12:7

75. Widen E, Factor-Litvak P, Gallagher D, Paxton A, et al. The pattern of gestational weight gain is associated with changes in maternal body composition and neonatal size. Matern Child Health J. 2015; 19: 2286-2294

76. Josefson JL, Simons H, Zeiss SM, Metzger BM. Excessive gestational weight gain in the first trimester among women with normal glucose tolerance and resulting neonatal adiposity. Journ of Perinatology. 2016; 36: 1034-1038

77. Crume TL, Shapiro ALB, Brinton JT, Glueck DH, Martinez M, Kohn M, Harrod C, Friedman JC, Dabela D. Maternal fuels and metabolic measures during pregnancy and neonatal body composition: the Healthy Start study. J Clin Endocrinol Metab. 2015: 100(4):1672-1680

78. McKenzie K, Dissanayake H, McMullan R, Caterson I, et al. Quantity and quality of carbohydrate intake during pregnancy newborn body fatness and cardiac autonomic control: conferred cardiovascular risk? Nutrients. 2017; 9:1375

79. Moore BF, Sauder KA, Starling AP, Hebert J, et al. Proinflammatory diets during pregnancy and neonatal adiposity in the Healthy Start study. J Pediatr. 2018;195:121-7.

80. Brei C, Stecher L, Meyer DM, Young V, Much D, Brunner S, Hauner H. Impact of dietary macronutrient intake during early and late gestation on offspring body composition at birth, 1, 3 and 5 years of age. Nutrients 2018; 10, 579

81. Thornburg K. The maternal nutritional mulieu and neonatal outcomes: connecting the dots. The Journal of Pediatrics. 2017

82. Chia AR, Tint MT, Han CY, et al. Adherence to a healthy eating index for pregnant women is associated with lower neonatal adiposity in a multiethnic Asian cohort: the Growing Up Singapore Towards healthy Outcomes (GUSTO) study. Am J Clin Nutr. 2018;107:71-79.

83. Bayol SA, Simbi BH, Bertrand JA et al. Offspring from mothers fed a 'junk food' diet in pregnancy and lactation exhibit exacerbated adiposity that is more pronounced in females. J Physiol. 2008;586:3219-3230

84. Azad MB, Sharma AK, de Souza R, DOlinsky VW, et al. Association between artificially sweetened beverage consumption during pregnancy and infant body mass index. JAMA Pediatr. 2016;170 (7):662-670.

85. Hardy L. Commentary: intrauterine exposure to artificially sweetened beverages and offspring adiposity: is this the tip of the iceberg? International Journal of Epidemiology. 2017;46:5.

86. Pereira-da-Silva L, Cabo C, Moreira AC, Papoila AL, Virella D, Neves R, Bridges KM Cordeiro-Ferreria G. The effect of long chain polyunsaturated fatty acids intake during pregnancy on adiposity of healthy full term offspring at birth. Journal of Perinatology. 2015;35: 177-180.

87. Tint MT, Chong MF, Izzuddin AM, Godfrey KM, et al. Association between maternal mid-gestation vitamin D status and neonatal abdominal adiposity. Int J of Obesity 2018; 42: 1296-1305

88. Ludwig, DS. Technology, diet and the burden of chronic disease. JAMA. 2011;305:13

89. Swinburn BA, Sacks G, Hall K, McPherson K, et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet. 2011; 378:804-813.

90. Vandevijvere S, Chow CC, Hall KD, et al. Increased food energy supply as sa major driver of the obesity epidemic: a global analysis. Bull World Health Organ. 2015;93:446-456.

91. Monteiro CA, Moubarac JC, Cannon G, Ng SW, Popkin B. Ultra-processed products are becoming dominant in our system. Obesity Reviews. 2013;14:21-28

92. Monteiro C, Cannon G, Moubarac JC, et al. The UN decade of nutrition, the NOVA food classification and the trouble with ultra-processing. Public Health Nutrition 2017;21:1.

93. Fardet A. Minimally processed foods are more satiating and less hyperglycemic than ultra-processed foods: a preliminary study with 98 ready to eat foods. Food Funct. 2016;7:2338-2346

94. Juul F, Hemmingsson E. Trends in consumption of ultraprocessed foods and obesity in Sweden between 1960 and 2010. Public Health Nutrition. 2015;18:7

95. Fiolet T, Srour B, Sellem L, et al. Consumption of ultra-processed foods and cancer risk: results from the NutriNet-Sante prospective cohort. BMJ. 2018;360:k322

96. Da Costa Louzada ML, Bortoletto Martins AP, Silva Canella D, et al. Impact of ultra-processed foods on micronutrient content in the Brazilian diet. Rev. Saude Publica. 2015;49:45

97. Batal M, Johnson-Down L, Moubarac JC, et al. Quantifying associations of the dietary share of ultra-processed foods with overall diet quality in First Nations peoples in the Canadian provinces of British Columbia, Alberta, Manitoba and Ontario. Public Health Nutrition 2017; 21:1

98. Crino M, Barakat T, Trevena H, Neal B (2017) Systematic Review and Comparison of Classification Frameworks Describing the Degree of Food Processing. Nutr Food Technol 3(1): doi http://dx.doi.org/10.16966/2470-6086.138

99. Khandpur N, Monteiro C. Nutrient based warning labels may help in the pursuit of healthy diets. Obesity 2018;26:11.

100. Monteiro CA, Cannon G, Moubarac JC, Levy RB, et al. Ultra-processing: an odd appraisal. Public Health Nutrition. 2017;21:3

101. Martinez Steele E, Baraldi LG, et al. Ultra-processed foods and added sugars in the US diet: evidence from a national representative cross-sectional study. BMJ Open. 2016;6:e009892

102. Martinez-Steele E, Raubenheimer D, Simpson SJ, et al. Ultra-processed foods, protein leverage and energy intake in the USA. Public Health Nutrition. 2017;21:1

103. Eicher-Miller H, Fulgoni V, Keast D. Contributions of processed foods to dietary intake in the US from 2003-2008: a report of the Food and Nutrition Science Solutions Joint Task Force of the Academy of Nutrition and Dietetics, American Society for Nutrition, Institute of Food Technologists and International Food Information Council. J. Nutr. 2012;142:2065S-2072S

104. Tseng M, Neil D, Teaford SF, Nazmi A. Alternative MyPlate menus: effects of ultra-processed foods on saturated fats, sugar and sodium content. JNEB. 2018;50.

105. Schwingshackl L, Bogensberger B, Hoffman G. Diet Quality as assessed by the healthy eating index, alternate healthy eating index, dietary approaches to stop hypertension score and health outcomes: an updated systematic review and meta-analysis of cohort studies. Jour. Acad. Nutr Diet. 2018;118:1

106. Kirkpatrick S, Reedy J, Krebs-Smith SM, et al. Applications of the healthy eating index for surveillance, epidemiology, and intervention research: considerations and caveats. Jour. Acad. Nutr. Diet. 2018;118:9

107. Schap T, Kuczynski K, Hiza H. Healthy Eating Index- beyond the score. Jour Acad Nutr Diet. 2017;117:4

108. McCullogh ML, Willet WC. Evaluating adherence to recommended diets in adults: the alternate healthy eating index. Public Health Nutrition. 206;9;152-157

109. Liese A, Krebs-Smith S, Subar A, George SM, et al. The dietary patterns methods project: synthesis of findings across cohorts and relevance to dietary guidance. Jour Nutr. 2015;

110. Lavigne-Roubachard M, Moubarac JC, Latagne-Lopez D, et al. Diet quality indices in relation to metabolic syndrome in an Indigenous Cree (EEyouch) population in norther Quebec, Canada. Public Health Nutrition. 2017;21:1

111. Weaver, CM, Dwyr J, Fulgoni V, King J, Leveille G, et al. Processed Foods: contributions to nutrition. Am J Clin Nutr 2014;99:1525-42

112. Asfaw A. Does consumption of processed foods explain disparities in the body weight of individuals? The case of Guatemala. Health Econ. 2011; 20:184-195

113. Hull H, Thornton J, Ji Y, et al. Higher infant body fat with excessive gestational weight gain in overweight women. Am J Obstret Gynecol 2011, 205:211e.1-7

114. Fairburn, CG, Berglin SJ. Assessment of eating disorders: Interview or self-report questionnaire? Int J Eat Disord 1994;6:1-8.

115. Beck, AT, Steer RA, Brown GK. BDI-II Manual. 1996, San Antonio, TX: Harcourt Brace and Company.

116. Knowler, WC< Barrett-Connor E. Fowler SE< e al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403

117. Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes Care 2007:30:1374-83.

118. Hilson JA, Rasmussen KM, Kjolhede CL. Maternal obesity and breast feeding success in rural population of white women. Am J Clin Nutr 1997:66:1371-8.

119. Subar A, Kirkpatrick S, Mittle B, et al. The automated self-administered 24 hour dietary recall (ASA24): a resource for researchers, clinicans and educators from the National Cancer Institute. J Acad Nutr Diet 2012, August; 112(8): 1134-1137. Doi:10.106/j.and/2012.04.16

120. Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: what they are and how to identify them. *Public Health Nutrition*. 2019;22(5):936-941. doi:10.1017/S1368980018003762

121. Urlando, Dempster, and Aitkens, "A New Air Displacement Plethysmograph for the Measurement of Body Composition in Infants."

122. Deierlein A, Thornton J, Hull H, Paley C, Gallagher D. An anthropometric model to estimate neonatal fat mass using air displacement plethysmography Nutrition and Metabolism 2012, 9:21

123. Gallagher D, Belmonte D, Duerenberg P, et al. Organ-tissue mass measurement allows modeling of REE and metabolically active tissue mass. Am J Physiol 1998; 275:E249-58.

124. Andres A, Gomez-Acevedo H, Badger T. Quantitative nuclear magnetic resonance to measure fat mass in infants and children. Obesity 2011, 19: 2089-2095. Doi: 10.1038/oby.2011.215

125. Abu-Bader SH. (2011) Advanced and Multivariate Statistical Methods for Social Science Research Chicago Illinois Lyceum Books Chapter 1, 2, 4, 5, 8

126. Maxwell, S. E. & Delaney, H. D. (2004). Designing Experiments and Analyzing Data: A Model Comparison Perspective(2nd ed.).

127. Laerd Statistics (2015). *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

128. Laerd Statistics (2016). Chi-square test for association using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

129. Laerd Statistics (2016). Chi-square test for independence using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

130. Laerd Statistics (2015). Independent-samples t-test using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

131. Laerd Statistics (2018). Spearman's correlation using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

132. Laerd Statistics (2018). Pearson's product-moment correlation using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

133. Laerd Statistics (2015). Binomial logistic regression using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

134. Laerd Statistics (2015). Simple linear regression using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved from https://statistics.laerd.com/

135. Fung TT, Pan A, Hou T, et al. Food quality score and the risk of coronary artery disease: a prospective analysis in 3 cohorts. *Am J Clin Nutr*. 2016;104(1):65–72. doi:10.3945/ajcn.116.130393

136. Posner B, Martin-Munley S., Smigelski C, Cupples L, Cobb J, Schaefer E. Comparison of Techniques for Estimating Nutrient Intake: The Framingham Study. *Epidemiology 1992 3*(2), 171-177.

137. Pawlak MT, Alvarez BT, Jones DM, Lezotte DC. The effect of Race/Ethnicity on gestational weight gain. *Journal of Immigrant and Minority Health*. 2015;17(2):325-332. http://ezproxy.cul.columbia.edu/login?url=https://search.proquest.com/docview/1664982572?accountid=10226. doi: http://dx.doi.org/10.1007/s10903-013-9886-5.

138. Dorsey K, Thornton JC, Heymsfield SB, Gallagher D. Greater lean tissue and skeletal muscle mass are associated with higher bone mineral content in children. Nutrition & Metabolism 2010 7:41 doi 10.1186/1743-7075-7-41

139. Hall KD. Ultra-processed diets cause excess calorie intake and weight gain: A one-month inpatient randomized controlled trial of ad libitum food intake. Doi: 10..31232/osf.io/w3zh2.

140. Cade JE. DIET@NET: best practice guidelines for dietary assessment in research. BMC Medicine 2017 15:202 DOI 10.1186/s12916-017-0962-x

142. Fardet A, Lakhssassi S, Briffaz A. Beyond nutrient-based food indices: a data mining approach to search for a quantitative holistic index reflecting the degree of food processing and including physicochemical properties. Food Funct. 2017 doi: 10.1039/c7fo01423f

Appendix: NOVA Categorization

Firstly, the correct FNDDS database must be selected to be run with the sample ASA24 data. This is version 4.1. This database, which contains the nine digit food codes, was brought into Stata from Excel and merged with the corresponding Main Food Description file. The files were merged three times to create the necessary spaces for the following merges. The next merge was to bring in the NOVA categories. Each food code from FNDDS is matched with one of the four NOVA categories. If the food code requires further information, as in additional ingredients, four or five digit SR codes were used to complete the classification. For example, the food code for a ready to drink meal replacement is **11560020**; there is nothing more for the NOVA classification file to read. However, if the product is sold in powdered form and requires the addition of a liquid, an example of that food code is **11612000** which prompts the classification file to also search for and use additional SR codes (such as milk). For example:

****116 Milk-based meal replacements, fluid: Group 4; Subgroup "Milk-based drinks";**
replace FC_nova_group=4 if (Food_code_3d==116|dr12ifdcd==11560020)
replace FC_nova_subg=37 if (Food_code_3d==116|dr12ifdcd==11560020)
replace fc_or_sr="f" if (Food_code_3d==116|dr12ifdcd==11560020)

***use SR_codes if dr12ifdcd==11612000 ("Instant breakfast, powder, milk added")**
replace FC_nova_group=12 if (dr12ifdcd==11612000)
replace FC_nova_subg=37 if (dr12ifdcd==11612000)
replace fc_or_sr="s" if dr12ifdcd==11612000

If something was coded as replace fc_or_sr="s" then another merge was performed with an NOVA for SR file which looked like the text below.

***Cream, sour: Group 2; Subgroup "Fats" (sg16)**
replace SR_nova_group=2 if (SR_code_t==1055|SR_code_t==1056)
replace SR_nova_subg=16 if (SR_code_t==1055|SR_code_t==1056)
***Sour cream: reduced fat, fat free, light: Group 4; Subgroup "Others" (sg41)**

replace SR_nova_group=4 if (SR_code_t==1178|SR_code_t==1179|SR_code_t==1180)
replace SR_nova_subg=41 if (SR_code_t==1178|SR_code_t==1179|SR_code_t==1180)

Below are some examples of how similar products could be coded into different NOVA

categories:

**114 Yogurt
//"Yogurt, plain," (FC=11411010/ 11411100/ 11411200/ 11411300): Group 1; Subgroup "Milk and plain yoghurt"
replace FC_nova_group=1 if Food_code_5d==11411
replace FC_nova_subg=9 if Food_code_5d==11411
replace fc_or_sr="f" if Food_code_5d==11411

//"Yogurt, NFS,": Group 4; Subgroup "Milk-based drinks";
replace FC_nova_group=4 if Food_code_5d==11410
replace FC_nova_subg=37 if Food_code_5d==11410
replace fc_or_sr="f" if Food_code_5d==11410

// Flavoured and fruit yogurts: Group 4; Subgroup "Milk-based drinks";
replace FC_nova_group=4 if Food_code_4d==1141 & dr12ifdcd==11410000
replace FC_nova_subg=37 if Food_code_4d==1141 & dr12ifdcd==11410000
replace fc_or_sr="f" if Food_code_4d==1141 & dr12ifdcd==11410000

replace FC_nova_group=4 if (Food_code_4d==1142|Food_code_4d==1143|Food_code_4d==1144)
replace FC_nova_subg=37 if (Food_code_4d==1142|Food_code_4d==1143|Food_code_4d==1144)
replace fc_or_sr="f" if (Food_code_4d==1142|Food_code_4d==1143|Food_code_4d==1144)

//"Frozen yogurt": Group 4; Subgroup "Ice cream, ice pops and frozen yogurts"
replace FC_nova_group=4 if (Food_code_4d==1145|Food_code_4d==1146)
replace FC_nova_subg=25 if (Food_code_4d==1145|Food_code_4d==1146)
replace fc_or_sr="f" if (Food_code_4d==1145|Food_code_4d==1146)

****123 Sour cream**
***Sour Cream: Group 2; Subgroup "Fats"**
replace FC_nova_group=2 if Food_code_4d==1231 & dr12ifdcd==12310100
replace FC_nova_subg=16 if Food_code_4d==1231 & dr12ifdcd==12310100
replace fc_or_sr="f" if Food_code_4d==1231 & dr12ifdcd==12310100

***Sour cream: reduced fat, fat free, light: Group 4; Subgroup "Others"**

***replace FC_nova_group=4 if Food_code_4d==1231 & dr12ifdcd!=12310100**
*replace FC_nova_subg=41 if Food_code_4d==1231 & dr12ifdcd!=12310100
*replace fc_or_sr="f" if Food_code_4d==1231 & dr12ifdcd!=12310100
replace FC_nova_group=4 if Food_code_4d==1231 &
(dr12ifdcd==12310300|dr12ifdcd==12310350|dr12ifdcd==12310370)
replace FC_nova_subg=41 if Food_code_4d==1231 & (
dr12ifdcd==12310300|dr12ifdcd==12310350|dr12ifdcd==12310370)
replace fc_or_sr="f" if Food_code_4d==1231 &
(dr12ifdcd==12310300|dr12ifdcd==12310350|dr12ifdcd==12310370)

***Sour cream: imitation (nondairy) (12320100); , filled, sour dressing, nonbutterfat (12320200): Group 4; Subgroup "Others"**
replace FC_nova_group=4 if (dr12ifdcd==12320100|dr12ifdcd==12320200)
replace FC_nova_subg=41 if (dr12ifdcd==12320100|dr12ifdcd==12320200)
replace fc_or_sr="f" if (dr12ifdcd==12320100|dr12ifdcd==12320200)

After foods were classified into NOVA categories using the food codes or SR codes, then subsequent information from the FNNDS database was also merged including moisture and fat content of food item at consumption to account for weight and nutrient value data from the SR codes. After the template of NOVA categorization was complete with all corresponding data affecting energy intake or food weight, the sample data food codes were merged and food code data not matched to a subject identifier was dropped from the dataset, leaving only sample pertinent information. This then allowed for the data to be analyzed for NOVA category contributions to the diet in the context of energy intake and food weight. Each participant was given a category percentage at pre intervention and post intervention and finally the covariate data was merged in to create the data file to be analyzed for the aims in this dissertation.