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iThe Importance of Nutrition in Pregnancy and Lactation: Lifelong Consequences

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Condensation: This manuscript covers the importance of nutrition in supporting a healthy pregnancy and the controversies, questions and research gaps regarding appropriate nutrient intake during pregnancy.

Short title: Nutrition in Pregnancy: Lifelong Consequences

Keywords: adolescent pregnancy; developmental origins of disease, fetal and neonatal nutrition; gestational diabetes; lactation; macronutrients; maternal nutrition; nutritional requirements; pregnancy; micronutrients; vitamin supplementation

Abstract:

The majority of women in the United States do not meet recommendations for healthful nutrition and weight before and during pregnancy. Women and providers often ask what a healthy diet for a pregnant woman should look like. The message should be "eat better, not more." This can be achieved by basing diet on a variety of nutrient dense, whole foods, including fruits, vegetables, legumes, whole grains, healthy fats with omega-3 fatty acids including nuts and seeds, and fish, in place of poorer quality highly processed foods. Such a diet embodies nutritional density and is less likely to be accompanied by excessive energy intake compared to the standard American diet consisting of increased intakes of processed foods, fatty red meat, and sweetened foods and beverages. Women who report "prudent" or "health conscious" eating patterns before and/or during pregnancy may have fewer pregnancy complications and adverse child health outcomes. Comprehensive nutritional supplementation (multiple micronutrients plus balanced protein energy) among women with inadequate nutrition has been associated with improved birth outcomes, including decreased rates of low birthweight. A diet that severely restricts any macronutrient class should be avoided,

specifically the ketogenic diet that lacks carbohydrates, the Paleo Diet due to dairy restriction, and any diet characterized by excess saturated fats. User-friendly tools to facilitate a quick evaluation of dietary patterns with clear guidance on how to address dietary inadequacies and embedded support from trained health care providers are urgently needed.

Recent evidence has shown that although excessive gestational weight gain (GWG) predicts adverse perinatal outcomes among women with normal weight, the degree of pre-pregnancy obesity predicts adverse perinatal outcomes to a greater degree than GWG among women with obesity. Low body mass index and insufficient gestational weight gain are also associated with poor perinatal outcomes. Observational data have shown that first trimester gain is the strongest predictor of adverse outcomes. Interventions beginning in early pregnancy or pre-conception are needed to prevent downstream complications for mothers and their children. For neonates, human milk provides personalized nutrition and is associated with short- and long-term health benefits for infants and mothers. Eating a healthy diet is a way for lactating mothers to support optimal health for themselves and their infants.

Introduction:

The reproductive period is a critical time for establishing risks of later life chronic disease in offspring.[1] Nutrition plays a vital role during this developmental period and because it is a determinant of lifetime risk for disease, it is potentially a modifiable risk factor. Although the World Health Organization (WHO) provides guidelines for antenatal care,[2] comprehensive guidelines detailing nutritional needs of women throughout reproduction from pre-conception through pregnancy and lactation are lacking.

The role of optimal nutrition for the continuum beginning at preconception, during pregnancy, at birth and beyond extending through childhood and adolescence has received too little attention from researchers, clinicians, and policy experts in the past, but has recently become a frequent topic of discussion, including a recent National Academies of Science, Engineering, and Medicine workshop.[3] The need for additional well designed research on this topic became apparent in a recent series of systematic reviews from the U.S. Department of Agriculture (USDA): Nutrition Evidence Systematic Review, Pregnancy and Birth to 24 Months Project.[4] Twenty-nine of the most important questions related to pregnancy and infant milk-feeding practices were systematically reviewed, with the highlights related to nutrition during pregnancy presented in **Figure 1**. Each topic was summarized by a conclusion statement and was assigned a grade based on quality of evidence. For five conclusion statements, a grade was not assignable, and the remaining three pregnancy questions received a grade that reflected only limited available evidence.[5,6] For the infant milk topics, four received a grade indicating moderate evidence, ten had limited evidence, and a grade was not assignable for 21 questions.[7]

The uncertain conclusions of the above mentioned systematic reviews underscore the need for more well-conceived studies to address specific questions regarding the role of nutrition in pregnancy. However, the inadequate numbers of studies able to meet the strict criteria of the reviews do not negate the large number of robust studies on related topics from which the scientific community can glean benefit. In this review, we have included such studies that give important insight on the many aspects of nutrition for women during their reproductive years.

In the past, public policy guidelines did not include pregnant or lactating women or infants under age two. Fortunately, the 2020-2025 Dietary Guidelines for the first time include recommendations for infants, toddlers, and pregnant women that will provide added benefit for health care professionals and the public. The USDA released its final guideline document (USDA 2020-2025 Dietary Guidelines) in December 2020. [8] Although this report was not available at the time of the *Nutrition in Pregnancy: Lifelong Impact* conference in 2019 which was the motivation for this review, the findings and recommendations of this document are nevertheless consistent with the new USDA guidelines.[9] Other reviews on this topic bring additional clarity to the issue.[10]

The conclusions offered herein come from recommendations from assembled experts on 1) the health benefits of consuming nutritious food before, during, and following pregnancy, 2) the value of promoting improved nutrition among pregnant women, and 3) the gaps in knowledge regarding nutrition during reproductive years that require urgent attention. While the meeting was largely focused on women in the United States, there were also important insights from global partners.

Points of agreement of authors:

1. Comprehensive improvements in nutrition and health status of women prior to conception and during pregnancy will contribute to optimal fetal growth, favorable obstetrical outcomes, improved perinatal survival, and the potential for better long-term health in both mother and offspring.

2. Poor maternal nutritional status is causally associated with abnormal fetal growth patterns including low birthweight (LBW – less than 2500g), small for gestational age (SGA) (<10% birthweight for gestational age)/fetal growth restriction (FGR), macrosomia (>4-4.5 kg), and large for gestational age (LGA) (>90% birthweight for gestational age), each of which is associated with increased risks for development of childhood and adult chronic diseases.

3. The dietary patterns of pregnant adolescents are generally less healthy than those of pregnant adult women and are critically important during a time of continued maternal growth and development, indicating the need for enhancing diet quality among young pregnant mothers. Many adolescent mothers face multifaceted socioeconomic and lifestyle difficulties that require professional and social support to aid in optimizing their diets, as well as other aspects of their health and social care, before, during and after their pregnancies.

4. The consumption of a beneficial dietary pattern before and during pregnancy is associated with a reduced risk of disorders of pregnancy, including gestational diabetes mellitus (GDM), pre-term birth, obesity-related complications, and in some populations, preeclampsia and gestational hypertension. Nutrition therapy provides the foundation for

treatment of GDM and is especially important for pregnant women with obesity, who have undergone bariatric surgery, or who have pre-existing diabetes.

5. A diet with balanced macronutrient intake provides the best chance for a healthy pregnancy and optimal perinatal outcomes. Nutritious diets are those that include ample quantities of vegetables, fruits, whole grains, nuts, legumes, fish, oils enriched in monounsaturated fat, and fiber, and are lower in fatty red meat and refined grains. Healthy diets also avoid simple sugars, processed foods, and trans- and saturated fats.

6. A diet that consistently and substantially restricts any macronutrient should be avoided during pregnancy. Fad diets as promoted by the popular press are widespread and may be especially harmful during pregnancy due to resulting nutrient imbalance and consequent nutrient deficiencies or ketosis.

7. Growing evidence indicates that maternal pre-pregnancy BMI impacts the influence of GWG on complications of pregnancy. While the optimal time to improve maternal body weight and nutrition-related lifestyle is well before conception occurs, GWG goals including a diet that limits non-nutritive, calorie dense foods may be more achievable intervention targets for some women than modifying weight before pregnancy.

8. Human milk is uniquely suited to meet nutritional needs of normal infants born at term for the first four to six months of life, and its consumption during infancy is associated with lower chronic disease risks in later life. Human milk composition is influenced by maternal dietary intake during lactation as well as maternal adipose nutrient stores, which together influence maternal milk/nutrient production and composition. Among women with GDM, there is evidence that exclusive breastfeeding for at least 6 months decreases the risk of Type 2 diabetes for the mother and is protective for the risk of childhood obesity in her offspring.

9. The regular consumption of multi-vitamin and mineral supplements that contain optimal amounts of folic acid, among other micronutrients, is recommended for all reproductive-age women to augment a balanced diet, starting at least 2-3 months before conception and continuing throughout pregnancy until the cessation of lactation or at least 4-6 weeks postpartum. Women who become pregnant after bariatric surgery need additional supplements and close monitoring before and during pregnancy.

10. It is imperative that health care providers have the time, knowledge and means to discuss optimal nutrition and provide educational support to women of reproductive age in order to improve their health before, during and after pregnancy.

A review of the scientific bases for points of agreement are explained below.

1. Comprehensive improvements in nutrition and health status of women prior to conception and during pregnancy will contribute to optimal fetal growth, favorable obstetrical outcomes, improved perinatal survival, and the potential for better long-term health in both mother and offspring.

Background and Current status:

Recent national data suggest that many women in the United States do not meet recommendations for healthful weight and nutrition before and during pregnancy. As of 2019, 29% of women met criteria for obesity prior to pregnancy, which increased by 11% from 2016. Overall, only 32% of US women gain weight within the recommended range during gestation, and the distributions of low or excessive weight gain vary accordingly by pre-pregnancy BMI.[11] In 2015, only half of US women surveyed met guidelines for physical activity and 29.7% reported taking a vitamin/folate supplement regularly before pregnancy.[12] National data on food intake in US women before and during pregnancy women is limited, but several reports suggest that sub-standard quality diets are common.[13-16] For example, between 2010-13, a cohort of 7500 nulliparous women from 8 large US medical centers recalled their usual diet within 3 months of conception and researchers assessed their diet quality using the Healthy Eating Index 2010.[14] More than half of the women reported inadequate number of servings of the component food groups. The authors estimated that 39% of calories came from foods containing added sugars, solid fats and alcohol, and the mean Healthy Eating Index Score was only 63 out of 100 points.[14] When the same index was estimated for 795 pregnant participants in the National Health and Nutrition Examination Survey (NHANES), 2003 to 2012, the score was lower (poorer diet quality) at 50.7.[13] In another recent analysis of pregnant women in NHANES, more than a third reported diets below the Estimated Average Requirement for key nutrients like vitamin D, E, iron, and magnesium, even with use of dietary supplements, while 99.9% reported diets too high in sodium.[16]Social disadvantage plays a role in food behavior and researchers have identified characteristics of US women such as education level below a college degree and women of color who may be at highest risk for less healthy intakes[13-15] or low levels of nutritional biomarkers.[13,17]

Impact on Pregnancy Outcomes

Twentieth century researchers and clinicians considered the fetus to be “a perfect parasite”[18] who could meet its nutritional requirements in all but extreme famine.[19] This perspective encouraged pregnant women to restrict their diet and minimize GWG in the middle 20th century.[20] Low birthweight infants were assumed to be “skinny” but “relatively untroubled”.[19] However, current evidence finds that maternal body size, dietary practices, and nutritional status before and during pregnancy are important factors for fetal health. Both inadequate and excessive nutrition, and weight prior to and during pregnancy, contribute to complications related to fertility (maternal and paternal), conception, development of the placenta, embryo, and fetus, fetal size and perinatal complications, resulting in suboptimal pregnancy consequences for mother and infant. [14,21-27] (**Table 1**). Animal models and human studies suggest that maternal nutrition and maternal pre-pregnancy metabolic condition regulate fetal-placental gene expression, organ structures, metabolism, and growth during critical periods of development, affecting offspring risk of cardiovascular, metabolic, respiratory, immunologic, neuropsychiatric and other chronic conditions starting during childhood development and into adulthood, with and without LBW.[28-31] The intrauterine environment can establish poor trajectories of health that may be increased when nutrient restriction *in utero* is followed by postnatal nutrient excess.[32,33] To illustrate, in Holland during World War II, where the population recovered from the Dutch Hunger Winter famine relatively quickly, exposure to the famine early in pregnancy was associated with higher risk of offspring obesity and cardiovascular disease in adulthood, whereas exposure to famine in the second half of pregnancy led more commonly to type 2 diabetes.[32]

<u>*Opportunities for Positive Impact*</u>

Unfortunately, recognition of the importance of preconception nutrition, with the exception of micronutrients such as folate for prevention of neural tube defects, is limited among health care workers, policy makers, and the public. The WHO report of the commission on Ending Childhood Obesity recognized preconception and pregnancy care as one of 6 key areas of action and called for clear guidance and support for the promotion of good nutrition and dietary counseling in antenatal care.[34] Although healthy eating and physical activity counseling for adequate weight gain is recommended, the availability of effective support during pregnancy is limited. Weight gain in pregnancy in low- and middle- income countries (LMIC) is not monitored routinely in some countries, and pre-pregnancy BMI is generally unknown. In addition, culturally acceptable, affordable, nutritious food supplements are urgently needed in areas where the prevalence of maternal undernutrition and poor food quality is high. Comprehensive improvements in nutrition and health status of women prior to conception and during pregnancy may have immediate effects on fetal growth, obstetric outcomes and perinatal survival. In a recently completed multi-country trial in which the effects of a comprehensive nutrition intervention initiated prior to conception was compared to the same intervention initiated late in the first trimester (vs. no intervention), birth outcomes, including birth length and weight, LBW, SGA, and stunting, were strongly impacted by the nutritional intervention, with the largest effects in the preconception arm.[35] Nulliparity and preconception anemia were strong effect modifiers of the response to intervention with more modest effects by baseline BMI. [35,36] The WHO global guidance for antenatal care recommends several central nutritional and health interventions for a healthy pregnancy, including multiple micronutrient supplements containing iron-folic acid, calcium supplementation for prevention of preeclampsia in low intake contexts, and balanced energy and protein supplementation for undernourished populations to reduce low birthweight.[2]

For women with easy access to low-quality food and who are overweight or have obesity, evidence to support preconception nutrition is insufficient and mostly observational. Limited evidence suggests a specific benefit of a diet higher in vegetables, fruits, whole grains, nuts, legumes, and fish, and lower in red and processed meats before and during pregnancy, being associated with a reduced risk of hypertensive disorders of pregnancy and GDM.[5] Overweight and obesity are a major public health problem affecting more than two-thirds of women of reproductive age. [37,38] Limited studies have shown improvement in maternal diet following preconception lifestyle interventions,[39,40] but the field of published preconception prospective interventional trials remains severely lacking.[41]

2. Poor and inappropriate maternal nutritional status is causally associated with abnormal fetal growth patterns including low birthweight (LBW – less than 2500g), small for gestational age (SGA) (<10% birthweight for gestational age)/fetal growth restriction (FGR), macrosomia (>4-4.5 kg), and large for gestational age (LGA) (>90% birthweight for gestational age), each of which is associated with increased risks for development of childhood and adult chronic diseases.

Background and Status

Examples of the powerful influence of maternal nutrition on fetal development are demonstrated by the pregnancy outcomes associated with neonates at the extremes of birthweight: 1) neonates below the 10th percentile in weight for gestational age at birth are defined as SGA and 2) neonates born exceeding the 90th percentile in weight-for-age are defined as LGA. These birthweights represent, in part, the nutritional status of the mother before and during pregnancy but do not necessarily reflect infant body composition (lean and fat mass).[42] One of the WHO's global nutrition targets calls for a 30% reduction in LBW.[43] A recent *Lancet* paper estimates 20.5 million infants will be born LBW globally; thus progress toward achieving the target has been slow.[44] Maternal nutritional status including low and high pre-pregnancy BMI, inadequate weight gain, short stature, anemia and micronutrient deficiency are causally associated with LBW which may be a result of preterm birth, impaired fetal growth, or both.

Impact of Maternal Nutrition on Pregnancy Outcomes

During extremes of maternal undernutrition, the fetus develops chronic fetal growth restriction (FGR),[45,46] a prime example of "survival at the expense of growth." This phenotype includes decreased pancreatic growth, development, and insulin secretion; increased capacity for glucose uptake in peripheral tissues (such as skeletal muscle);[47] reduced utilization of amino acids for protein synthesis and cell growth; and development of hepatic insulin resistance with increased glucose production in an ovine model that produced hypoxia in the fetus as well as reduced nutrient supply.[48] We now know that the FGR phenotype, especially when followed by later life excess caloric intake, is a risk for development of obesity, insulin resistance, and diabetes later in life.[49,50] Unfortunately, no strategies have emerged that improve growth and development of the FGR fetus once diagnosed in pregnancy. Previous attempts (maternal oxygen supplementation, bed rest, augmented nutrition, medications) either have not worked or caused harm.[51] As a result, current management of FGR pregnancies involves fetal surveillance and delivery of the fetus when adverse physiology becomes apparent, in hopes that the FGR neonate can be treated more effectively outside the uterus.[52] While there is no direct nutritional strategy for treating FGR, recent studies in sheep reveal that uteroplacental gene therapy involving vascular endothelial growth factor safely increased fetal growth velocity and reduced the incidence of FGR.[53] In addition, recent data indicate that nutritional support and exercise before pregnancy may be more efficacious in promoting healthy placentation and fetal growth than during pregnancy.[54] The current postnatal strategy in which infant weight is a primary criterion for neonatal intensive care unit/hospital discharge may also contribute to excessively rapid catch-up growth, especially for body fat mass, as parents and providers are motivated to align newborn intake and nutrition to meet weight gain targets rather than maintaining normal fetal *in utero* growth trajectories.[55,56]

At the other extreme, fetal overnutrition from maternal obesity, diabetes, and high fat and sugar intake may result in macrosomia/LGA.[57] These conditions that present excess glucose and lipid supply to the fetus are increasingly common and associated with numerous complications. Fasting as well as pulsatile postprandial hyperglycemia promotes fetal insulin secretion, contributing to excess glycogen storage and fat accretion in the fetus, especially in pregnancies complicated by type 2 diabetes and GDM as well as type 1 diabetes, particularly when complicated by obesity.[58] Although pregnancies complicated by diabetes are commonly associated with macrosomia and/or LGA, the majority of cases of these infants are born to mothers with obesity alone, which now affects up to 1 out of 3 women.[37] Even greater fetal fat mass accumulation occurs with the combination of high maternal plasma glucose and lipid concentrations.[58-60] Recent evidence suggests that maternal triglycerides, made available to the fetus by placental lipases that hydrolyze the triglycerides to free fatty acids (FFA), are primary drivers of fetal fat mass growth in pregnancies with obesity and contribute to accelerated fat mass accumulation in the fetus.[58,61,62] Fetuses have limited capacity for fatty acid oxidation[63,64] but can store fat. Excess fat mass accreted in utero might contribute to later obesity, but clearly postnatal fat mass accretion especially during the first one to two years of life can persist into later life leading to obesity in childhood. In a non-human primate model, a maternal Western style diet (WD) resulting in intermittently higher postprandial glucose and lipid exposure to the fetus resulted in the three-year old offspring demonstrating higher glucose excursions. Furthermore, the juveniles' pancreatic islets secreted more insulin, suggesting that these islets were primed before birth to hyper-secrete insulin.[65] In contrast, extremely high and relatively constant glucose concentrations in the fetus actually can suppress insulin production and response to glucose stimulation.[66] This, along with abnormal placentation and decreases in placental perfusion may explain why some women with long-standing type 1 diabetes complicated by vascular disease will have neonates who are SGA, but who are also at increased risk for later metabolic disease, especially when exposed to an obesogenic envirnoment.[19,66]

There is increasing evidence that persistent, very high fetal glucose concentrations can inhibit fetal neuronal development, leading to reduced neuronal number, dendritic proliferation, and synapse formation, ultimately leading to reduced cognitive function in such offspring later in their lives.[67] In humans, a recent study in adolescent offspring from women with type 1 diabetes showed that cognitive function was significantly diminished, with lower intelligence scores and greater learning difficulties in the offspring whose mothers had more severe hyperglycemia associated with their diabetes.[68] Rates of congenital heart defects and major malformations of the central nervous system derived from the neural tube, such as caudal regression syndrome, are also higher in offspring of mothers with both Type 1 and Type 2 diabetes, and the risk period during organogenesis (<8 weeks) is often before women know they are pregnant.[69] However, stillbirth risk near term is highest in mothers with Type 2 diabetes, especially when associated with obesity,[70,71] both conditions associated with excess maternal caloric intake and malnutrition.

Maternal overnutrition also plays an important role in the early origins of childhood obesity, as well as inflammatory diseases such as Non-Alcoholic Fatty Liver Disease (NAFLD), the most common liver disease worldwide affecting 1 in 3 youth with obesity.[72] A "multiple-hit" pathogenic model has been suggested to explain the progressive liver damage that occurs among children with NAFLD.[73] Data in humans demonstrate that liver fat is 68% higher in neonates born to mothers with obesity and GDM, and is strongly correlated with maternal pre-pregnancy BMI and perhaps, maternal triglycerides before subcutaneous fat stores are fully developed.[74,75] Moreover, evidence from the national pediatric non-alcoholic steatohepatitis (NASH) network, shows that high or low birthweight, even when adjusting for childhood BMI, doubles the risk for advanced fibrosis in youth with biopsy confirmed NAFLD,[76] suggesting that changes at birth may precede and possibly predict the rapid onset of NASH in at-risk youth for reasons that remain poorly understood. Without effective treatments, children with NASH are at risk of developing cirrhosis and liver-related mortality in early adulthood.

Opportunities for Positive Impact:

All women of childbearing age should receive pre-conception counseling and guidelines on nutrition, physical activity, and optimal GWG, with particular attention to those with undernutrition or overnutrition, those with a pre-pregnancy BMI that indicates underweight, overweight, or obese status, those with medical complications including diabetes, prediabetes, insulin resistance, a history of GDM, chronic hypertension, and any chronic medical disease (cardiopulmonary, obstructive sleep apnea, rheumatologic, NAFLD, gastrointestinal, etc.). Medical management of any chronic condition should be optimized prior to pregnancy and women should be provided with options for effective contraception until the timing of pregnancy is optimal.

3. **The dietary patterns of pregnant adolescents are generally less healthy than those of pregnant adult women and are critically important during a time of continued growth and development, indicating the need for enhancing diet quality among young pregnant mothers. Many adolescent mothers face multifaceted socioeconomic and lifestyle difficulties that require professional and social support to aid in optimizing their diets, as well as other aspects of their health and social care, before, during and after their pregnancies.**

Background and current status

The physiology of pregnancy may differ in adolescents from that in adult pregnant women. Young maternal age (particularly <16 years) is a significant risk factor for stillbirth, preterm delivery, LBW, and neonatal mortality.[77-81] The probability of these adverse outcomes is greatest when pregnancy coincides with continuing and/or incomplete growth of the adolescent mother.[82,83] Sheep paradigms involving nutritional management of weight and adiposity in young biologically immature adolescents have replicated this competition for nutrients between mother and offspring in the womb.[84-86] Although poor nutrient reserves at conception do play a modest role, dietary manipulation of the maternal growth trajectory during pregnancy has the most profound impact on pregnancy outcomes. Overfeeding adolescent sheep to promote rapid maternal growth during pregnancy is particularly detrimental. It leads to abnormal placental growth/development, reduced uteroplacental blood-flow, and reduced fetal nutrient delivery.[87] In the sheep model, these lead to high rates of premature delivery of LBW lambs and increased rates of intrauterine growth restriction (IUGR).[88] In addition, initial lactation is impaired and neonatal morbidity is high. In contrast, when maternal growth after conception is prevented by under-feeding adolescent sheep, the progressive depletion of the mother's nutrient reserves results in only a small reduction in birthweight independent of any change in placental size or length of gestation.[85] Appropriate caloric intake maintains maternal adiposity throughout gestation, and this optimises feto-placental growth and birth-outcomes. Maternal and placental endocrine systems are differentially altered in both over- and undernutrition with downstream effects on fetal endocrine systems, organ development and body composition.[85] Approaches to reverse these effects in sheep have been explored: notably, improving nutrition during late-gestation in the undernourished model restores fetal nutrient supply, normalizes fetal adiposity and partially restores birthweight.[84,89] Following delivery, growth-restricted lambs of both sexes born to over-fed adolescents and who are fed according to appetite have an altered metabolic and body-composition phenotype which persists into adulthood[90] whereas offspring of underfed adolescent sheep are largely unaffected.

Impact on Pregnancy Outcomes

This body of work using sheep models has public health implications for human adolescents living in both low and high-income countries. Adolescents have been found to consume higher levels of snack and processed foods, less fruit and vegetables, and take fewer nutritional supplements compared to adult women.[91] Irrespective of geographical location, both nutrient reserves at conception and gestational dietary intake are likely to be powerful determinants of fetal growth in very young girls whose own growth is still ongoing or incomplete.[92] Data from human pregnancies in adolescent mothers with respect to over- and under-nutrition remains limited.[35,93]

Opportunities for Positive Impact

In settings where women have chronically inadequate diets, intervening during pregnancy has shown limited benefit in perinatal outcomes.[94,95] Intervention strategies among poorly nourished women are more effective if initiated months before conception.[96] Adolescent nutrition has been neglected, particularly in LMIC.[93] The Lancet Commission on Adolescent Health drew attention to both over- and undernutrition burden in this age group that comprises about 18% of the world's population.[97] As adolescent girls have not historically been prioritized in global research, there is a significant data gap regarding the burden of underweight and stunting within adolescent girls in LMIC and the knowledge of interventions needed to optimize this period of rapid growth and development.[92,98]

High-energy nutritional intakes that promote rapid maternal growth during pregnancy in adolescents may constrain placental development and function and are potentially more detrimental than restricted nutritional intakes that prevent maternal growth.[99] In areas where early marriage soon after menarche is the norm, there is evidence that girls with a low BMI should be advised to gain weight and achieve a normal BMI before conception to decrease the risk of preterm birth and neonatal underweight.[100] Thereafter dietary intakes should be sufficient to maintain maternal nutrient reserves throughout pregnancy. Where pregnancies are unplanned and food is readily available, biologically immature mothers and caregivers should be aware of the potential consequences of excessive GWG with respect to placental development. Monitoring of placental size and uteroplacental blood flow may help identify those at risk of perinatal complications but is not yet of proven efficacy.

4. **The consumption of a beneficial dietary pattern before and during pregnancy is associated with a reduced risk of disorders of pregnancy, including GDM, pre-term birth, obesity related complications, and in some populations, preeclampsia and gestational hypertension. Nutrition therapy provides the foundation for treatment of GDM and is especially important for pregnant women with obesity, who have undergone bariatric surgery, or who have pre-existing diabetes.**

Gestational Diabetes

Nutrition therapy is the foundation for treatment of GDM. Rooted in carbohydrate restriction, the rationale for this approach can be traced to the pre-insulin era, when restriction of carbohydrate to ≤10% of calories was among few interventions that could prolong life in those with Type 1 diabetes.[101,102] Pioneers in the field of diabetes in pregnancy recognized that in-utero environmental conditions that influence fetal growth are shaped by maternal nutrition.[103] Moreover, contemporary evidence in the previous 2-3 decades has supported associations between fasting and postprandial glucose and infant birthweight, solidifying the need for control of maternal glucose to prevent fetal overgrowth in pregnancies affected by diabetes.[104] With restriction of dietary carbohydrate comes the risk of increasing dietary fat intake due to replacement of carbohydrate with fat calories, particularly in obesogenic environments influenced by easy availability of processed foods and low-carbohydrate fad diets promoted by the popular press.[105] At the same time, mounting evidence supports that high saturated fat diets result in elevated free fatty acids, which inhibit insulin signaling and result in insulin resistance[106] which may increase fetal exposure to excess nutrients. Furthermore, fetal exposure to excess maternal lipids, especially triglycerides, is linked with fetal overgrowth and excess adiposity, both potent predictors of later childhood obesity and metabolic disorders.[58,102,107] In 2005, the American Diabetes Association acknowledged the concern for excess fetal lipid exposure secondary to maternal diet, de-emphasizing restriction of carbohydrate,[108] and worldwide, there is no consensus on the optimal approach to treatment of GDM with nutrition therapy.[109,110]

When a woman receives a diagnosis of GDM, regardless of the exact diagnostic criteria, nutrition therapy is the first line of treatment.[111] There is high hope across the field that nutrition therapy alone in the absence of adjunct treatment with insulin or oral diabetes agents can effectively and economically treat the growing number of women with GDM. Data that are more recent underscore metabolic similarities in patterns of glycemia and lipidemia between diet-controlled GDM and maternal obesity *without* GDM.[112,113] This highlights an opportunity to more thoughtfully target women with obesity outside of GDM for treatment with nutrition. The importance of good nutrition for all pregnant women was also recently highlighted by data demonstrating strong associations between fasting and postprandial triglycerides and neonatal adiposity in both women with normal-weight and obesity (without GDM), further supporting a role for targeting these nutrition sensitive indicators.[60] Unfortunately, randomized controlled trials using diet and lifestyle changes, although resulting in slightly less GWG, have overall not been successful in preventing GDM.[114]

Currently, evidence does not support one particular nutritional approach to treatment of GDM. In fact, it was recently shown that, globally, advice for nutrition in GDM is mixed between carbohydrate restriction and more liberal carbohydrate intake, with focus instead on choosing low glycemic index foods, consumption of more complex carbohydrates, increasing dietary fiber and limiting consumption of saturated fats.[115] The quality of the available evidence is poor, with high heterogeneity across studies, lack of control for confounding medications, poor reporting of GWG, and low dietary compliance.[109,111] Very recently, a controlled trial in which women with GDM were randomized to a lower carbohydrate, higher fat (40% carbohydrate; 45% fat) diet versus a higher complex carbohydrate diet (60% carbohydrate, 25% fat) (both eucaloric and all meals provided for the duration of pregnancy) found no differences in birthweight, newborn adiposity by PeaPod, or cord C-peptide supporting that complex carbohydrate can be liberalized by 20% above conventional recommendations and similarly normalize fetal growth, expanding nutrition options in GDM.[116] A recent meta-analysis across 18 randomized-controlled trials (RCTs) and 8 diet patterns for nutrition in GDM demonstrated that any modification which improves nutritional quality and intake following GDM diagnosis is effective in reducing fasting and postprandial glucose, and lowering infant birthweight.[117]

Pregnancy after Bariatric-Metabolic Surgery

Preconception weight loss for women with obesity holds great promise to improve maternal and fetal health but is difficult to achieve through lifestyle alone. On the other hand, bariatric-metabolic surgery (currently the most common being Roux-en-Y gastric bypass and, recently, sleeve gastrectomy) can result in total weight loss averages that approach 25-30% with accompanying benefits in, and often resolution of, most obesity-related comorbidities, including GDM.[118] Greater numbers of women with severe obesity are now undergoing bariatric-metabolic surgeries and subsequently are becoming pregnant. Although meta-analyses of study outcomes of this population of mothers have typically demonstrated favorable outcomes with regard to lower rates of hypertensive disorders of pregnancy (62% lower), GDM (80% lower), and fewer babies born LGA (69% fewer); they have also reported a slight increase in pre-term delivery (Odds Ratio [OR]: 1.35) and a higher likelihood of SGA (OR: 2.16), especially when compared to women matched for pre-surgical BMI.[119] The close timing of bariatric surgery with respect to subsequent pregnancies in addition to the type of surgery are likely important risk factors for SGA. Because women are in an active weight loss phase during the first year after bariatric surgery, pregnancy should be avoided.[120] Furthermore, micronutrient deficiencies such as iron, Vitamin D, and Vitamin B12 deficiencies are common in patients who have undergone bariatric surgery, especially with Roux-en-Y gastric bypass, and must be adequately resolved before and during pregnancy. Less clear are the longer-term ramifications of these post-surgical maternal weight, metabolic, and micronutrient changes on infant and childhood development as well as their risk for chronic diseases of adulthood (e.g., obesity, diabetes, and cardiovascular disease), however the lower risk of GDM and LGA would appear to confer a benefit.

Preeclampsia and Preterm Delivery

The pathophysiology of preeclampsia is believed to be related to poor placentation accompanied by oxidative and endoplasmic reticulum stress in placental cells in addition to abnormal angiogenesis.[121] These processes may be modifiable by nutrition, and hence a good deal of attention has been directed to the role of nutrition in preeclampsia. Unfortunately, these concepts have not been well studied and in many cases, conclusions have been diametrically opposed (overnutrition[122] vs. undernutrition,[123] too much[124] vs. too little[125] dietary salt. etc.) Current information on diet has recently been thoroughly reviewed[5] (see Figure 1) and the role of micronutrients in preeclampsia is a subject of increasing scrutiny. Yet due to the challenges of studying the role of nutrition in the prevention of preeclampsia, their relationship remains largely unresolved. In four studies of nutrition before and during pregnancy to modify preeclampsia and gestational hypertension risk, limited data suggested a reduced risk with a diet higher in vegetables, fruits, whole grains, nuts, legumes, fish, and vegetable oils and lower in meat and refined grains. This information was from healthy Caucasian European women with access to medical care.[5] Data were insufficient to estimate this relationship in minority women or women of low socioeconomic status.

Micronutrient studies have provided a few helpful insights regarding their role in the prevention of preeclampsia. Calcium supplementation has been shown to be useful in settings with low calcium intake, leading to the conclusion that replacement, not supplementation, is relevant.[126] Therapy with Vitamin C and E as administered in several large studies has not proven effective to prevent preeclampsia.[127,128] Several other micronutrients including folic acid,[129,130] Vitamin A and D,[130] zinc,[131] iodine,[132] omega 3 fatty acids[133] and arginine[134] are supported by some by not all supplementation studies. A meta-analysis restricted to LMIC reported a significant effect of omega-3 supplementation on preeclampsia (RR 0.40, 95% CI: 0.21-0.77, I^2 0%, six studies, N=1343), but there was no difference in severe preeclampsia, eclampsia, or gestational hypertension.[133] There are also some intriguing possibilities that deserve further studies, including periconceptional vitamins,[135-137] dietary nitrates,[138] reduced sodium intake[139] and antioxidants other than vitamins C and E, but thus far none have been of proven benefit.[140]

Omega-3 supplementation reduced the risk of early preterm delivery at < 34 weeks (RR 0.42, 95% CI 0.27-0.66, p=0.0002, 6 studies, n=4193) and any preterm birth (RR 0.83, 95% CI 0.70-0,98, p=0.03, 9 studies, n=5980) according to a systematic review. The effect persisted on sensitivity analysis when restricted to women with spontaneous preterm birth (RR 0.44, 95% CI 0.25-0.78, p=0.005). [141]

5. A diet with balanced macronutrient intake provides the best chance for a healthy pregnancy and optimal perinatal outcomes. Nutritious diets are those that include ample quantities of vegetables, fruits, whole grains, nuts, legumes, fish, oils enriched in

monounsaturated fats, and fiber, and are lower in fatty red meat and refined grains. Healthy diets also avoid simple sugars, processed foods, and trans- and saturated fats.

Systematic reviews suggest that, compared to the standard American diet consisting of highly processed foods, fatty red meat, and sweetened foods and beverages, women who report “prudent” or “health conscious” patterns before and/or during pregnancy (seafood, poultry, whole grains, legumes, healthy fats, and fruits and vegetables), may have fewer pregnancy complications and adverse infant and child health outcomes.[5,6,142-147] One study of couples who consumed a Mediterranean diet during IVF cycles found an increased probability of pregnancy (OR 1.4, 95%CI 1.0-1.9).[148] However, large randomized controlled trials would add more specific recommendations, although it is clearly improper to randomize women to diets preconception and during pregnancy if one diet is viewed as less healthy.

As there continues to be significant misconceptions about the safety of seafood intake during pregnancy, leading some pregnant women to avoid seafood all together, it is important to emphasize the 2015-2020 Dietary Guidelines for Americans, supported by the US. Food and Drug Administration and the Environmental Protection Agency, which recommend that women who are pregnant or breastfeeding consume between 8 to 12 ounces of a variety of seafood per week from choices that are lower in mercury (see Figure 3).[149] Low mercury fish choices include salmon, pollock, flounder, cod, tilapia, shrimp, oysters, clams, scallops and clams. Fish provide important nutrients including proteins, healthy omega-3 fats, iron, and vitamins B12 and D, among others.

Omega-3 free fatty acids can also be obtained through algae-based supplements, flax, hemp, and walnuts. Although seaweed is another source, iodine content can vary and may be excessive,[150,151] and seaweed can contain environmental contaminants depending on where it is grown.[152]

6. **A diet that consistently and substantially restricts any macronutrient should be avoided during pregnancy. Fad diets as promoted by the popular press are widespread and may be especially harmful during pregnancy due to resulting micronutrient deficiency or ketosis.**

Significant imbalance of macronutrient intake may be associated with harm. As examples, pre-pregnancy carbohydrate restriction has been associated with higher odds for neural tube defects (aOR 1.30, 95% CI 1.02-1.67), although the data are limited by design.[153] Further, restriction of dietary carbohydrates elevates the risk of increasing dietary fat intake to replace calories lost, and high levels of saturated fats increase free fatty acids and insulin resistance.[105,116,154] Offspring of mothers on a low carbohydrate diet may be prone to gain weight in childhood, which may be epigenetically driven.[155] Fetal exposure to excess lipids is linked to fetal overgrowth and excess adiposity, predictors of later childhood obesity and metabolic disorders.[58-60] A ketogenic diet often minimizes carbohydrates and promotes the consumption of high protein, high fat foods that may be harmful;[111] extremes of protein intake have been associated with low birthweight.[156] Placental-fetal glucose demands are thought to approach 150 grams/day in later pregnancy, and recent data suggest that placental glucose consumption is higher than previously understood.[157] Low carbohydrate diets promote increased lipolysis and may promote starvation ketosis in pregnancy with unknown consequences to the fetus.[105,107,111,112] The Paleo diet promotes consumption of excess saturated fats and restricts consumption of dairy-based foods, which may contribute to deficiencies in calcium and vitamin D, and the single published study of 76 women in pregnancy suggested possible improvements in glucose tolerance and anemia but was associated with lower birthweight.[158] Maternal diet quality was recently shown to have some effect on infant adiposity at birth,[159] but further studies and biomarkers are clearly needed to better characterize maternal diet quality and its effect on newborn body composition.

7. Growing evidence indicates that maternal pre-pregnancy BMI impacts the influence of GWG on complications of pregnancy. While the optimal time to improve maternal body weight and nutrition-related lifestyle is well before conception occurs, GWG may be a more achievable intervention target for some women than modifying weight before pregnancy.

Gestational weight gain: a critical appraisal of the Institute of Medicine (IOM) guidelines

In 2009 the US IOM released evidence-based recommendations for optimal weight gain across pregnancy according to maternal pre-pregnancy weight status that have been broadly adopted by both clinicians and researchers in the US and elsewhere.[160] Recent evidence has shown that among women with obesity, the degree of pre-pregnancy obesity predicts adverse outcomes for a pregnancy to a greater degree than does GWG.[161] This adds more urgency to targeting interventions to help women achieve the healthiest possible weight prior to and between conceptions.[21] Nonetheless, there is also evidence that low weight gain, especially in underweight or normal weight women, or excessive gestational weight gain is associated with adverse maternal and child outcomes.[162,163] Opportunities offered during prenatal care for pregnant women may be a more feasible intervention compared to helping women optimize their weight pre-pregnancy.[25]

In the US, measurement of weight is routine at each prenatal care visit. This practice however is not consistently found in all other countries,[164] and even in the US, real-time patient feedback and counseling related to weight tracking is not routinely practiced.[165] Clinicians continue to identify insufficient time and knowledge related to counseling best practices as barriers to improving weight-related tracking and counseling.[166] Furthermore, in generating weight gain guidelines, the IOM committee did not have adequate evidence to identify specific advice by subclasses of obesity. They therefore recommended at least 5 kg of weight gain for all women entering pregnancy with a BMI >30 kg/m^2, regardless of obesity class. Epidemiological data published since then suggest that the ideal gestational weight gain varies by obesity class. For obesity grade I (BMI 30-34.9 kg/m^2) and II (BMI 35.0-39.9 kg/m^2), studies suggest that maternal gains less than the lower limit of the IOM recommendation may not increase adverse outcomes and may, in fact, decrease LGA and GDM,[161,163,167] while other studies indicate an increased risk of SGA and infant mortality with weight loss and very low weight gain.[168-170] However, for women with obesity grade III (BMI ≥40.0 kg/m^2), lower levels of gain, or even weight loss, may be optimal, but the current evidence is observational and based on weight alone, not maternal diet or lifestyle behaviors.[168,170,171]

Due to insufficient evidence at the time, the 2009 guidelines also did not provide evidence-based recommendations regarding diet or physical activity changes that would best help women to achieve recommended gains. The recent evidence report and systematic review for the US Preventative Services Take Force (USPSTF) found that counseling and active behavioral interventions to limit GWG were associated with lower risk of GDM, macrosomia, LGA, and emergency cesarean delivery, as well as reduced GWG of -1.02 kg.[172] This led the USPSTF to issue a new recommendation statement that clinicians offer pregnant persons effective behavioral counseling interventions aimed at promoting healthy weight gain and preventing excessive GWG in pregnancy (B recommendation).[173]

As the IOM guidelines focused on high resource settings, low resource settings may need different standards to support women who are underweight and have low GWG. In LMICs, improved GWG (100g/wk) was associated with significantly improved birthweight and length, as was baseline pre-pregnancy BMI, early weight gain, and GWG from 12-32 weeks.[174]

8. **Human milk is uniquely suited to meet nutritional needs of normal infants born at term for the first four to six months of life, and its consumption during infancy is associated with lower chronic disease risks in later life. Human milk composition is influenced by maternal dietary intake during lactation as well as maternal adipose nutrient stores, which together determine maternal milk/nutrient production and composition. Among women with GDM, there is evidence that exclusive breastfeeding for at least 6 months decreases the risk of Type 2 diabetes for the mother and is protective for the risk of childhood obesity in her offspring.**

Human milk provides personalized nutrition and is associated with long-term health benefits for infants and mothers. [175,176] According to the 2012 American Academy of Pediatrics policy statement, "Given the documented short- and long-term medical and neurodevelopmental advantages of breastfeeding, infant nutrition should be considered a public health issue and not only a lifestyle choice."[176] Milk composition is influenced by maternal dietary intake during lactation as well as maternal adipose nutrient stores, which together are then responsible for the nutrients available for milk biosynthesis, and ultimately maternal milk/nutrient production.[177] In order to meet all infant nutritional needs, human milk is constantly changing, composition varies by infant age, between breasts, within a feed, throughout the day, over the course of lactation, among women, and among populations. In light of these significant variations, accurate assessment of milk composition remains a challenge for researchers. Evaluation of donor milk pools, assumed to come from women with adequate milk production to meet not only their infants' nutritional needs but with sufficient quantity to nourish other infants as well, show significant variation in composition. Among donor pools from the first and third quartiles, milk demonstrated up to a 33% difference in fat content, 22% difference in protein, and 16% difference in energy content.[178] Importantly, individual women show a greater difference in milk composition compared to variation by age of infant/length of time breastfeeding.[178,179]

Regarding individual macronutrients, maternal diet does not have a major impact on milk protein content or the total amount of fat in human milk, but does affect the types of fatty acids present in breast milk.[180,181] Maternal adipose stores remain an important source of nutrients for human milk, although women with greater fat mass do not produce more or higher fat milk.[182] Different lipids are the most variable component of human milk. Lipid composition variability is inversely related to the degree of breast fullness and milk volume. In addition to macronutrients and essential micronutrients, there is moderate evidence that flavors from the maternal diet during lactation are transferred into breast milk, and that infants are able to detect diet-transmitted flavors,[183] which may impact future taste preferences. The ratio of Omega-6 versus Omega-3 fatty acids in human breast milks appeared to promote postnatal fat development and this relationship requires further study.[184] Interestingly, human milk from women with obesity or Type 2 diabetes does not appear to expose the infant to a different macronutrient composition, but has been shown to have higher insulin levels and to influence the early infant microbiome population, but any effects on infant appetite or growth remain unclear.[185,186]

Women with GDM who breastfeed have decreased risk for developing type 2 diabetes mellitus (T2DM), with longer duration and increased intensity of breastfeeding associated with lower 2-year incidence of T2DM.[187,188] Breastfeeding is also associated with a decreased maternal risk for metabolic syndrome,[189] cardiovascular disease,[190] and cancer.[191] Unfortunately, women with overweight/obesity commonly experience difficulties in lactation and are less likely to be able to meet exclusive breastfeeding goals,[192] which suggests additional physiologic barriers.

9. The regular consumption of multiple micronutrient supplements that contain optimal amounts of folic acid, among other micronutrients, is recommended for all reproductive-age women to augment a balanced diet, starting at least 2-3 months before conception and continuing throughout pregnancy until the cessation of lactation or at least 4-6 weeks postpartum.

Evidence supports benefit of comprehensive nutritional supplementation (multiple micronutrients plus balanced protein energy) associated with improved birth outcomes of major public health interest (e.g. stunting, LBW, SGA).[193] This is supported by the 2020 WHO recommendation stating "antenatal multiple micronutrient supplements that include iron and folic acid are recommended in the context of rigorous research"[2] for pregnant women and adolescent girls. Preconception folic acid is recommended for prevention of neural tube defects.[194] Routine supplementation is adequate regardless of methylenetetrahydrofolate reductase geneotype.[195] A recent Cochrane systematic review provides evidence that a daily, multiple micronutrient supplement containing iron-folic acid vs. iron-folic acid alone significantly reduces LBW and SGA in LMIC.[196] Well-nourished women who consume an adequate diet may not require additional multi-vitamin supplementation, but in the absence of comprehensive evaluation by a dietitian, routine supplementation is encouraged in the US.[197] Subgroups that particularly warrant targeted interventions for improving nutrition include nulliparous women and those who are anemic. Anemia in non-pregnant women has recently increased in the US,[198] and is estimated to impact 38% of women on a global basis; prevalence is much higher (> 50%) in certain regions, including south Asia and central and west Africa.[199] Anemia prior to pregnancy and in the first trimester has been associated with preterm delivery and LBW.[200,201] Recently, a growing number of randomized controlled studies suggest that the supplementation of choline, especially in women with a history of alcohol use, may improve neurodevelopmental outcomes.[202-205] These findings underscore the need for revising the current policy and recommendations for supplement use in pregnancy as an adjunct to the nutritious diet described previously, as supplements alone cannot substitute for a healthy diet.

10. It is imperative that health care providers have the time and means to provide educational support and to discuss optimal nutrition with women of reproductive age in order to improve their health.

Transformative change is needed for addressing women and girls' nutrition as they hold roles in their communities that make them drivers of development as individuals, and influencers of the health and well-being of their families. Optimal reproductive health can be achieved when maternal nutritional wellbeing exists. This occurs only when known nutrition interventions are integrally linked to health programs and delivered at scale. Global commitment and political will are needed for driving this agenda forward. Conference experts emphasized the need for preventive health services for women, including nutrition advice over the entire reproductive cycle. They cite linkage of *individual* health behavior change and a supportive *policy/health care environment.*[206] Thus, greater efforts supporting interventions that provide wholesome nutrition and total micronutrient support are needed. This support will ensure that more women who will become pregnant will experience robust placentation and embryogenesis, resulting in lower disease risks in their offspring because of optimal epigenetic regulation of organs.[207]

Key Questions

Question 1: What are the unique nutritional requirements of a normal pregnant woman and what unique features of diets produce optimal health and growth of her fetus and infant?

The WHO defines good nutrition as "intake of food necessary for optimal growth, function and health. Good nutrition is defined as a well-balanced diet that provides all essential nutrients in optimal amounts and proportions, whereas poor nutrition is defined as a diet that lacks nutrients (either from imbalance or overall insufficient food intake) or one in which some components are present in excess."[208] Additional features of a healthy diet include foods that are accessible, acceptable, affordable, safe, culturally appropriate, and comprised of primarily whole foods consumed in moderation.

There is growing evidence that diet and nutritional status at preconception, starting as early as childhood and adolescence, appears to be equally or even more important[26] than during pregnancy, due to growing evidence that nutrition affects fertility and the early development of the placenta and fetus, which occur well before a woman recognizes that she is pregnant.[21] About half of US women of childbearing age consume unhealthy diets that are too high in processed ingredients, fat, sugar, and other refined carbohydrates and do not meet current nutritional recommendations.[13,14,16]

While it is commonly said that pregnant women are "eating for two", for most women, average energy requirements increase only modestly.[209] In contrast, assuming that the preconceptional diet was adequate, prenatal needs for some micronutrients, for example folate and iron, increase by one third to one-half respectively.[210] The WHO has declared iodine deficiency as the single most common cause of brain damage, after starvation, and mild iodine deficiency is still a public health concern in both developing countries and Western industrialized nations, especially Europe.[211] Iodine requirements increase in pregnancy and in nursing mothers to 250-300 ug per day (compared to 150 ug outside of pregnancy). These requirements begin very early due to the fetal need to synthesize thyroid hormone, critical for early neurogenesis, proliferation migration, differentiation, neurite outgrowth/guidance, synaptogenesis, and myelination. The fetal thyroid begins to concentrate iodine at 10-12 weeks gestation and begins making thyroid hormone with complete independence from maternal thyroid hormone production by 18 weeks.[212,213] It has been demonstrated that mild-moderate iodine deficiency, which is common in pregnancy, is associated with a 10-point decrease in total intelligence quotient score and an increase in attention deficit hyperactivity disorder in the offspring. [214]

Women and providers commonly ask what a healthy diet for a pregnant woman should look like and the message to US women should be "eat better, not more". This can be achieved by basing the diet on a variety of nutrient dense, whole foods, including fish, fruits, vegetables, omega 3 fatty acids and whole grains in place of poorer quality processed foods and beverages to enhance nutritional quality without excessive energy intake (Figure 2, **Table 2**) (USDA Dietary Guidelines). Maternal requirements vary by individual characteristics, and in addition to considering dietary quality prior to pregnancy, factors such as maternal body size, age, gestational age, multiple gestation, activity level and medical conditions should be considered. The USDA provides interactive online tools for health professionals to tailor dietary recommendations for women before and during pregnancy as well as the MyPlate interactive tool that women can use to plan their diets (https://www.choosemyplate.gov/browse-by-audience/view-all-audiences/adults/moms-pregnancy-breastfeeding). Table 3 offers the primary features of a healthy diet for discussing a healthy diet with patients and table 4 includes questions as conversation starters for health care providers when talking to patients.

(USDA MyPlate).

<u>Question 2: What is the optimal balance of macronutrients during pregnancy and lactation to support and maintain appropriate nutrient supply to the infant through lactation?</u>

Diet planning is especially important for women planning to conceive, throughout pregnancy, and during lactation. Dietary patterns are an evolving area of research that involves the entirety of the diet rather than focusing on individual nutrients or foods. There is limited but consistent evidence primarily in healthy White women with access to healthcare that dietary patterns before and during pregnancy higher in vegetables, fruits, whole grains, nuts, legumes, fish, and vegetable oils, and lower in meat and refined grains are associated with a reduced risk of disorders of pregnancy, including pre-eclampsia, gestational hypertension, GDM, and pre-term birth.[4-6] Conclusions about the association between dietary patterns during pregnancy and birthweight outcomes is less consistent and restricted by inadequate adjustment of birthweight for gestational age and sex variation in study design, lack of measures of infant body composition, dietary assessment methodology relying on recall rather than robust biomarkers of nutritional intake, and adjustment of key confounding factors.[6] However, in a recent cohort of 354 fully breastfeeding mother-infant dyads, in utero exposure to a higher quality maternal diet, based on the Healthy Eating Index-2015,[215] was inversely associated with percent of infant fat mass.[216] Avoidance of simple sugars, processed foods, trans- and saturated fats, and limiting red and processed meats is recommended. A diet that severely restricts any food group should be avoided, specifically the ketogenic diet that lacks carbohydrates, the Paleo Diet due to dairy restriction (promoting deficiencies in calcium and vitamin D), and any diet containing excess saturated fats. Foods with a high saturated fat content containing high omega 6 vs. omega 3 fatty acids constitute a pro-inflammatory diet, with some evidence of impact on obesity in the offspring and increased postnatal adipose tissue development.[184,217]

Literature on the effects of nutrition of lactating women on their infants' later health is scarce. Eating a healthy diet is a way for lactating mothers to support their health and the health of their infants during lactation. The quality of a mother's diet, particularly dietary fats including saturated vs. unsaturated fat, is an important way for mothers to ensure a healthy start for infant growth and development.

<u>*What is the best way to ensure that the embryo and fetus have adequate micronutrients over the course of gestation?*</u>

A balanced diet that includes fish twice a week for DHA, and whole grains for folate, vitamin B12, iron and choline is recommended as is supplementation of iodine by 150ug to ensure that pregnant women have a total intake of 250 ug/day.[212] For women with dietary restrictions, consultation with a nutritionist is recommended. A daily multi-vitamin that contains optimal amounts of folic acid and iron is recommended for women who are planning to become pregnant. Because only a small percentage of women will eat a complete diet that includes all required nutrients, appropriate dietary supplementation with optimal levels of iron and folic acid, as well as other micronutrients, is recommended. A dietitian may recommend other supplementation regimens for women at risk for insufficiency of specific micronutrients.

<u>Question #3: Should all pregnant women receive dietary assessment and personalized advice? If so, how can we educate a professional workforce to provide such advice?</u>

The relevance and practicality of routine nutritional assessment for all pregnant women has been the focus of debate among health care professionals, researchers and policy makers. The reluctance in providing universal nutritional assessment is partly due to resource and cost implications, but is in part due to the lack of robust evidence of effectiveness[4] or ambiguity about the acceptability of current nutritional assessment techniques among pregnant mothers and their care providers.[218]

However, in addition to the widely recognized critical role of nutritional health during gestation, pregnancy is seen as an opportune period to influence not only women's but also their families' lifestyle for healthier outcomes.[219] It is therefore important to assess pregnant women's nutritional status before or early in pregnancy in order to provide optimized care for mothers and their families.

Nutritional assessment during pregnancy

Nutritional assessments are carried out in various ways including anthropometric measurements, dietary intake evaluations, and assessment of blood biomarkers. Each of these approaches provides specific information on certain aspects of nutritional status and all have their limitations and advantages. Biochemical markers are direct ways of assessing adequacy of maternal nutrients and minerals. Although some biomarkers such as plasma hemoglobin levels are commonly screened as an indication of anemia, these tests are not routinely performed for all nutrients and minerals due to not being universally cost-effective or practical in most settings. Ferritin can be used to screen for iron deficiency, although the recommended cutoff for supplementation varies.[220] Furthermore, the assessment of dietary fatty acid ingestion reflected by mass spectrometry red blood cell (RBC) fatty acid (FA) analyses, which reflect 24 fatty acid species and polyunsaturated essential omega-6 and omega-3 fatty acid intake, are not usually performed in most studies although the analysis can now be done on a single blood spot and cost has become reasonable.[221-223] Assessing mothers' dietary intakes are also challenging requiring considerable amount of additional time, resource, knowledge and skills for practitioners. In addition to these challenges, most health care professionals who care for women during pregnancy are ill prepared to analyze dietary intake information and to provide appropriate advice and support to women when dietary inadequacies are identified.[224] Until there are user-friendly tools to facilitate a quick evaluation of dietary patterns with clear guidance on how to address dietary inadequacies and embedded support from trained health care providers, it is unlikely that nutritional assessments will become routine in clinical practice.

The most commonly used method of anthropometrics includes measuring weight and height at the first antenatal (booking) visit to calculate maternal body mass index (BMI) as an indicator of nutritional status. However, in some countries, follow-up weight assessments are not recommended or practiced, citing a lack of evidence on benefits of routine weighing during pregnancy, a lack of time or equipment, and concerns about anxiety that it may cause for mothers.[164] In a thematic analysis of 400 posts made in a UK-based parenting internet forums in the week following the publication of the National Institute for Health and Clinical Excellence

(NICE) guidance on weight management in pregnancy in July 2010,[225] concerns were expressed by women about feeling patronized if just being told about the risks of obesity and excessive gestational weight gain without clear guidance and support to manage it effectively.[226] The value of routine weight measurements during pregnancy without sensitive and helpful follow-up is thus a matter of debate by many health care professionals and investigators.[227,228]

Changes in the policies of governmental and professional organizations to improve nutritional health of women before, during and after pregnancy

The importance of maternal nutrition in relation to pregnancy health and intrauterine fetal growth and beyond is widely recognized. There is, however, a great deal of variation in policies and practices within and between countries concerning nutritional assessment and related care of women during the perinatal period. Numerous initiatives and organizations across the globe have attempted to address the growing nutritional challenges among maternity populations including National Academy of Medicine (formerly Institute of Medicine),[160] National Institute for Health and Care Excellence (NICE)[225], and Think Nutrition first.[26] There are also initiatives such as those in the UK "Every contact counts" with the aim of promoting healthy lifestyle at every opportunity in which patients/mothers attend clinics or visit health care providers.[229] There are, however, stark inconsistencies in recommendations and practices that are counterproductive in achieving optimum lifestyle and nutritional health during the reproductive period. A lack of sufficient evidence in clinically meaningful and/or locally sensitive and effective gestational weight management[4] approaches has been cited as a main reason for variation in current nutritional assessment and relevant care and management. Providing nutritional education and introducing interventions before pregnancy particularly from adolescent stages[230,231] through pregnancy and using digital sources for wider engagements are suggested.[232]

There is an urgent need for further research in providing culturally sensitive and effective interventions in promoting healthy lifestyle and reliable nutritional assessment over the perinatal period.

Question #4: How should we address the nutritional needs for special populations of women including those regularly consuming too many or too few calories or inadequate nutrients?

Special populations of women and pregnant women with unique nutritional needs have been identified to include adolescent girls, women with GDM, pregestational diabetes, overweight/obesity (particularly severe obesity), preeclampsia, and those women who are underweight. It is strongly recommended to develop strategies for targeting these special populations by individual groups to address the uniqueness of each condition.

Major research Gaps and Recommendations for Future Directions

The huge body of animal work, human observational studies, and a growing number of experimental trials aimed at understanding how maternal nutrition matters are exciting, but there are many challenges in conducting research in the field of nutrition among pregnant women. We are still in the early stages of accruing the kind of causal, consistent, nuanced data, preferentially based on more robust dietary biomarkers that are needed to confidently create interventions and policy.[28-30,233] Animal studies provide mechanistic explanations for the developmental features of imparting disease risk and associated epigenetic changes, but animal findings require demonstration in humans before they are applied clinically. This is particularly the case in adolescent pregnancies in which the human data are limited. Observational epidemiological studies with retrospective designs, such famine cohort studies and prospectively collected cohorts, have contributed tantalizing evidence supporting the animal work, but at best, they demonstrate correlative relationships because nutritional exposures often track with other social and environmental exposures. Diet is difficult to measure accurately, and the essential window of nutritional exposure may not be known or may vary by outcome studied. Even for well-designed prospective cohort studies, nutritional measures may begin after the critical window of exposure or may be limited to a single point in time, confounded by subjective measures of dietary recall, which does not reliably capture the full extent of a woman's intake or body weight. Maternal and child outcomes are multifactorial, making it difficult to identify the role of a particular exposure or the modifying effect of other exposures. Observational studies can be strengthened by new methods of analysis including use of sibling analyses that allow better control for shared genetics and environments. These approaches can better control for confounding, but still do not rise to the level of establishing clear causality.[233] Randomized controlled trials do allow for causal inference, but are often insufficient because the timing of the intervention that is feasible, such as the beginning of the second trimester, may miss the essential critical window of susceptibility. Moreover, studies are only able to focus on specific exposures during a limited time frame and are unable to control for subsequent exposures. At present, it is not possible to conduct experimental studies that allow sufficient time to follow participants over their lifetimes, nor to randomize women of childbearing age to what are perceived to be less healthy diets. It is equally difficult to demonstrate the chain of events from a maternal intervention (such as reducing excessive GWG) through the child's life course (assessing metabolic markers) to the ultimate outcome of obesity or chronic disease development during childhood, adolescence and adulthood given the innumerable and heterogeneous developmental exposures during the life course. Multigenerational studies should be established to ensure that such information is available for the next generation.

Future studies will bring new information on the roles of newly recognized areas of medicine, like the microbiome and diet, to the health of human offspring. The maternal microbiome is recognized as a key determinant of a range of important maternal and child health outcomes, and together with perinatal factors influences infant health [234]. The composition of the microbiome acquired in early infancy is critical for shaping infant and adult immune function and metabolic status.[235] The mechanisms by which intestinal dysbiosis in early life contribute to postnatal inflammation and progression of disease remain unclear. Metabolic plasticity has been proposed to underlie the observation that microbes not only critically contribute to initiation of inflammation and progression to childhood non-communicable diseases, including obesity, type I and type II diabetes, fatty liver disease, and even autism.[236] Personalized medicine is likely to substantially challenge the assumption that one diet fits all and demonstrate that recommendations on macronutrients and micronutrients do not affect every individual in the same way.[237] Given that diet is an environmental exposure that interacts with the genome, the epigenome and a person's individual metabolism, the field of personalized nutrition that takes into account the interactions between diet, genes and health using the approaches of nutrigenomics and nutrigenetics may become feasible to identify the optimal diet for an individual.[237]

Some studies suggest that pre/probiotics in pregnancy provide benefits;[238] however, the quality of evidence is weak as diet is simultaneously modified. Randomized clinical trials of pro- or prebiotics in pregnant women with obesity to date have shown little benefit on infant outcomes.[239] However, remodeling metabolic pathways during pregnancy or lactation due to changes in microbiome holds the promise for diminishing adverse developmental programming in the next generation.

Priority recommendations related to nutrition in pregnancy and lactation requiring the immediate attention of funding agencies were identified as follows:

Specific Major Gaps:

- Funding agencies should take an active role in directing the generation of high quality evidence relevant to nutrition in pregnancy. This may be accomplished through funding opportunities that require standardization across studies, control of confounders, and collection of common measures across studies and within specific populations, while ensuring enrollment of diverse populations for optimal generalizability. Funding agencies have the ability to request investigators to include specific variables and direct how they will be measured to increase the ability to compare studies/pool data in the future.
- Research projects that are designed to identify and validate nutritional biochemical markers to assess nutritional status are strongly recommended.

- Research is needed to understand the development of nutrigenomic-based approaches to identify ways to individualize nutrition recommendations.
- Research on the influence of the gut microbiome on maternal and infant health is emerging as a highly important area in order to increase our understanding of how manipulation through diet, human milk oligosaccharides (HMO's), and pre- or probiotics could influence perinatal outcomes.
- High quality studies of adolescent pregnancy and multiple gestations are needed to develop and implement effective nutritional strategies.
- A national policy group should be formed that includes representation from governmental, professional, academic and charity organizations to develop approaches that will promote the consumption of nutritious food among women before and during pregnancy and lactation.

The following strategies are recommended:

• Design evidence-based educational approaches that focus on nutrition across academic clinical programs for all providers in training, emphasizing a multi-disciplinary team approach to management.

• Design evidence-based education interventions focused on nutrition aimed at the public, both consumers and pregnant women and their families.

• Leverage advocacy groups to infuse evidence-based nutrition knowledge across public platforms.

• Leverage use of technology to disseminate appropriate nutrition education (Apps) and create connections between scientists, policy makers and the general population

- Fill a major gap in our understanding of fetal growth: to move beyond the limitations of our current ultrasound techniques to develop a simple approach during pregnancy to measure, accurately and repetitively and as non-invasively as possible, fetal growth, including length, head circumference, "weight", and body composition—as a minimum, lean vs. fat mass. Such methods would allow essential approaches to develop norms of fetal growth, to make such clinical measurements locally within unique populations and institutions, and to measure responses to different maternal diets and environmental conditions.
- Institute measures of maternal glucose concentration throughout pregnancy and for longer periods (e.g. continuous glucose monitors) to establish glycemic patterns. A major gap in the capacity to improve glucose metabolism and concentrations in the pregnant mother and avoid or reduce adverse impact on fetal growth and development is the lack of more continuous daytime and nocturnal measurements which could help maintain maternal glucose concentrations in the "normal" range and at "reasonably" constant levels for much longer periods. Considerably more studies are now in progress, indicating that this approach has the potential to improve current pregnancy management.[240-244]
- Implement better methods to assess lipid availability and use by the fetus which measure maternal lipid concentrations and profiles throughout pregnancy and for longer periods, including both fasting and postprandial triglycerides and RBC fatty acid profiles, the latter to characterize dietary intake of fatty acid, omega-6, and omega-3 polyunsaturated essential fatty acids. It also is important to determine how to maintain maternal lipid concentrations

in the "normal" range and at relatively constant concentrations with appropriate and successful maternal diets. Essential omega-3 fatty acids in the maternal diet should be emphasized with sufficient omega-6 fatty acids for fetal growth ensuring optimal neuronal development and brain growth. The longer-term consequences for later life metabolism and risk of adiposity, as well as neurological development and cognitive capacity, remain high priorities for future research.

- More clearly discern the normal amino acid and protein nutrition of the fetus given that the optimal maternal dietary protein content is not known. The regulatory roles of individual amino acids in the fetus need much clearer definition.
- Differentiate how to best feed the mother whose fetus and its placenta are showing signs of growth restriction (under-nutrition), and how to feed the mother whose fetus and placenta are showing signs of overgrowth of fat mass (over-nutrition) as early as possible in pregnancy.[245]

Gestational Diabetes Mellitus/Obesity

The following strategies are suggested to improve the outcome of pregnancies in women with GDM and/or obesity:

- Establish consensus across the field for diagnostic criteria and common priority measures in randomized controlled trials (RCTs), such as measurement of neonatal adiposity.
- Promote prospective planning with agreed upon clearly defined outcomes and adequate power estimates for multi-center trials.

- Establish consistent BMI reporting, including linking electronic medical record data for utilization of measured rather than reported maternal prepregnancy weight.
- Encourage consistent GWG reporting to include both total and pattern of GWG.
- Include, as appropriate, studies of women within all major ethnic groups and analyze as distinct groups (ethnicity, degrees of glucose intolerance, insulin resistance, abnormalities in insulin secretion) to mitigate metabolic heterogeneity.
- Use standardized treatments. The overall goal is balanced nutrition that is affordable and culturally acceptable for women with GDM,[111] as it should be for all pregnant women, which normalizes maternal weight and blood glucose concentrations. There should be increased representation of ethnically diverse women and women of lower socioeconomic status.
- Ascertain how individuals with different metabolic capacities might respond differently to dietary manipulation utilizing nutrigenomics specific to the mother, her microbiome, and potentially her fetus (personalized nutrition).

Future directions for preconception bariatric-metabolic surgery research include:

- Pregnancy outcomes by racial/ethnic status.
- Impact of micronutrient supplementation on maternal-fetal outcomes.
- Impact of specific bariatric surgeries, timing of surgery, and GWG and subsequent maternal-fetal outcomes.
- Mechanisms of increased risk for growth restricted infants.

- Effects on childhood development, growth, and expression of chronic diseases of adulthood.

Preeclampsia studies present special challenges, in addition to the usual challenges of nutritional studies. These suggests that successful studies:

- Should be done before pregnancy and in the periconceptional period. Many of the relevant nutritionally related developments of preeclampsia are present in very early pregnancy and some may be present before pregnancy.
- Require an accurate medical diagnosis that avoids confusion amongst the hypertensive disorders of pregnancy as well as self-reporting, as self-reporting of preeclampsia is very inaccurate (50-59% positive predictive value - PPV).[246]
- Should recognize the heterogeneous character and risk factors for preeclampsia and strive to consider "subsets."

Conclusions

There is consistent agreement that a woman's nutrition and weight should be assessed and improved before, during pregnancy, and after her pregnancy to encourage and promote the health of the woman and her offspring.[26,160,247,248] Thus, we must not wait for definitive scientific proof of mechanisms that underlie the potential beneficial effects of quality nutrition in a child-bearing woman before recommending nutrient rich diets before and throughout pregnancy and during lactation. It is the view of the authors that now is the time to assess our current knowledge of nutritional needs of women during their reproductive years, to apply what we know, generate public health policies that ensure nutritious food availability, and to strongly encourage funding agencies to prioritize nutritional research that will address the numerous knowledge gaps to improve health benefits to all populations.

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Tables:

Table 1. Outcomes linked to maternal weight and/or nutrition intake before or during pregnancy[21,22,25-27,30,147,160,194,196]

Maternal	Child
Fertility	Fetal malformations and loss
Oocyte and embryo quality	Preterm delivery
Antenatal, Intrapartum, and Postpartum Complications	Small for gestational age
Cesarean/operative delivery	Stillbirth
Lactation performance	Infant mortality
Depression	Rapid infant growth
Immediate and long-term obesity	Asthma and allergies
Development of non-communicable diseases over life course	Childhood obesity, adolescent, and adult obesity
	Early age of menarche

	Neurocognitive, mental, and behavioral health
	Altered DNA methylation
	Development of non-communicable diseases over life course

Table 2: Recommended Reproductive Diet Patterns

Name	Includes	Excludes	Benefits	Risks
Optimal diets				

Mediterranean diet (MD)	Plant-based foods – vegetables, fruits, whole grains, legumes, nuts, herbs, spices, olive oil, fish, poultry, red wine Up to 40% calories from fat	Limits red meat a few times per month	Lower CVD, mortality, cancers, cognitive disease	
Dietary Approaches to Stop Hypertension (DASH)	Balanced complex carbohydrates (58%), lower fat (28%), moderate protein (18%) High in fiber, calcium, phosphorus, magnesium, potassium	Low in cholesterol, fat, sodium	Weight loss, lower BP, improved cholesterol, lower CVD, lower bone loss	Needs vitamin D supplementation
Flexitarian Diet	Vegetarian most of the time, more vegetables, whole grains, plant-based/non-meat proteins (“new meat”), dairy, “sugar and spice”	Meat and dairy in moderation if at all	Lower BP, cholesterol, weight loss, heart disease, stroke diabetes	May need calcium, vitamin B12, iron supplementation

	Focus on home prepared with <5 ingredients			
Nordic Diet	Fruits, vegetables, legumes, potatoes, whole grains, nuts, seeds, rye bread, fish, seafood, low-fat dairy, herbs, spices, canola oil	Rare red meat and animal fats No sugar sweetened beverages, added sugars, processed meats, refined fast foods,	Weight loss, lower BP and inflammatory markers	
Diets to avoid during pregnancy				
Atkins Diet 20-40-100	Low carbohydrate (20 g), high fat, beef, pork, poultry, fish, eggs, cheese, sources of fat	Limit starchy vegetables, grains, legumes, simple sugars, milk		Needs vitamin C, B-vitamin including folate, calcium, magnesium

Paleo diet (PD)	Lean meats, fish, eggs, nuts, seeds, fruits, vegetables, oils	Processed foods, wheat, other grains, legumes, dairy, potatoes, refined sugar, salt, refined oils	Weight loss, lower risk diabetes, heart disease, cancer	Needs calcium, B-vitamins, whole grain nutrients
Ketogenic diet (KD)	Extreme carbohydrate restriction ketosis, skin-on poultry, fattier beef, pork, fish, green leafy vegetables, oils and solid fats	Avoid starchy root vegetables, bread, pasta, other grains, fruit	Weight loss	Not recommended in pregnancy due to altered neonatal brain development Needs vitamin C, B-vitamin including folic acid, calcium, fiber

Table 3

Common ground for healthy dietary patterns

• Whole, unprocessed foods and beverages
• Rich in fruits and vegetables
• Whole grains and complex carbohydrates, including ancient grains
• Healthy fats (mono and polyunsaturated), including nuts and seeds
• Healthy fish
• Plant-based protein
• Drink more water
• Lean meats and dairy products

Table 4

Nutrition conversation starters
• Tell me about the foods you usually eat.
• Are there foods that you tend to avoid?

• Do you prepare your own food?
• How many times a week do you eat foods that you didn’t prepare yourself?
• Do you think you eat a healthy diet? Why or why not?
• When asked about gestational weight gain, respond with “How do you feel about your food intake?” Strategize about ways to improve nutrition for maternal/fetal health AND appropriate GWG.
Food insecurity statements to ask
• Within the past 12 months, we worried whether our food would run out before we got money to buy more. • Within the past 12 months the food we bought just didn’t last and we didn’t have the money to get more.

Table 5: Glossary

Healthy Eating Index	A measure of diet quality used to assess how well a set of foods aligns with key recommendations of the Dietary Guidelines for American (https://www.fns.usda.gov/resource/healthy-eating-index-hei)

Estimated average requirement	A nutrient intake value that is estimated to meet the requirement of half the healthy individuals in a group (https://www.ncbi.nlm.nih.gov/books/NBK45182/)
Ketosis	A metabolic state in which fat provides most of the fuel for the body
Micronutrients	Vitamins and minerals required in trace amounts for the normal growth and development of living organisms
Malnutrition	Imbalanced nutrition
Nutrient dense	Food relatively rich in nutrients for the number of calories containedwhol
Undernutrition	Lack of proper nutrition, caused by not having enough food or not eating enough food containing substances necessary for growth and health
Overnutrition	A form of malnutrition arising from excessive intake of nutrients, leading to an accumulation of body fat that impairs health
Prebiotics	Foods that act as food for human microflora
Probiotics	Foods or supplements that contain live microorganisms intended to maintain or improve the normal microflora in the body.

Processed food	Food item that has had a series of mechanical or chemical operations performed on it to change or preserve it.
Whole foods	Food with little or no refining or processing and containing no artificial additives or preservatives; natural or organic food

Figure Legend

Figure 1: Dietary Patterns and Maternal and Birth Outcomes: Systematic Review results

Figure 2: My Pregnancy Plate

Figure 3: FDA and EPA Advice on Fish Consumption recommendations, revised July 2019

The Pregnancy and Birth to 24 Months Project (P/B-24), led by USDA and HHS, was a project in which USDA's Nutrition Evidence Systematic Review (NESR) team conducted a series of systematic reviews on diet-related topics of public health importance for women who are pregnant, infants, and toddlers.[27] NESR collaborated with an expert group focused on dietary patterns during pregnancy and 1) hypertensive disorders of pregnancy (HDP), 2) gestational diabetes mellitus (GDM), 3) gestational age and 4) birth weight.[7,8] NESR's systematic review methodology has been published.[246] A literature search was conducted and results were dual-screened to identity articles published from January 1980 to January 2017 that met predetermined criteria. For each included article, data were extracted, and risk of bias was assessed. The evidence was qualitatively synthesized, conclusion statements developed, and the evidence was graded. Complete documentation of each systematic review is available on the NESR website (https://nesr.usda.gov/pregnancy-technical-expert-collaborative-0). Below are excerpts from the conclusion statements for the four systematic reviews. Most of the conclusion statements received a grade of limited because of substantial methodological and measurement issues along with a lack of racial/ethnic diversity in the study samples.

Hypertensive Disorders of Pregnancy: Limited evidence in healthy Caucasian women with access to health care suggests that dietary patterns before and during pregnancy that are higher in vegetables, fruits, whole grains, nuts, legumes, fish, and vegetable oils and lower in meat and refined grains are associated with a reduced risk of hypertensive disorders of pregnancy, including preeclampsia and gestational hypertension. Not all components of the assessed dietary patterns were associated with all hypertensive disorders. (Grade: Limited)

Evidence is insufficient to estimate the association between dietary patterns before and during pregnancy and risk of hypertensive disorders of pregnancy in minority women and those of lower socioeconomic status. (Grade: Grade not assignable)

Gestational Diabetes Mellitus: Limited but consistent evidence suggests that certain dietary patterns before pregnancy are associated with a reduced risk of gestational diabetes mellitus. These protective dietary patterns are higher in vegetables, fruits, whole grains, nuts, legumes, and fish and lower in red and processed meats. Most of the research was conducted in healthy, Caucasian women with access to health care. (Grade: Limited)

Evidence is insufficient to estimate the association between dietary patterns during pregnancy and risk of gestational diabetes mellitus. (Grade: Grade not assignable)

Gestational age: Limited but consistent evidence suggests that certain dietary patterns during pregnancy are associated with a lower risk of preterm birth and spontaneous preterm birth. These protective dietary patterns are:

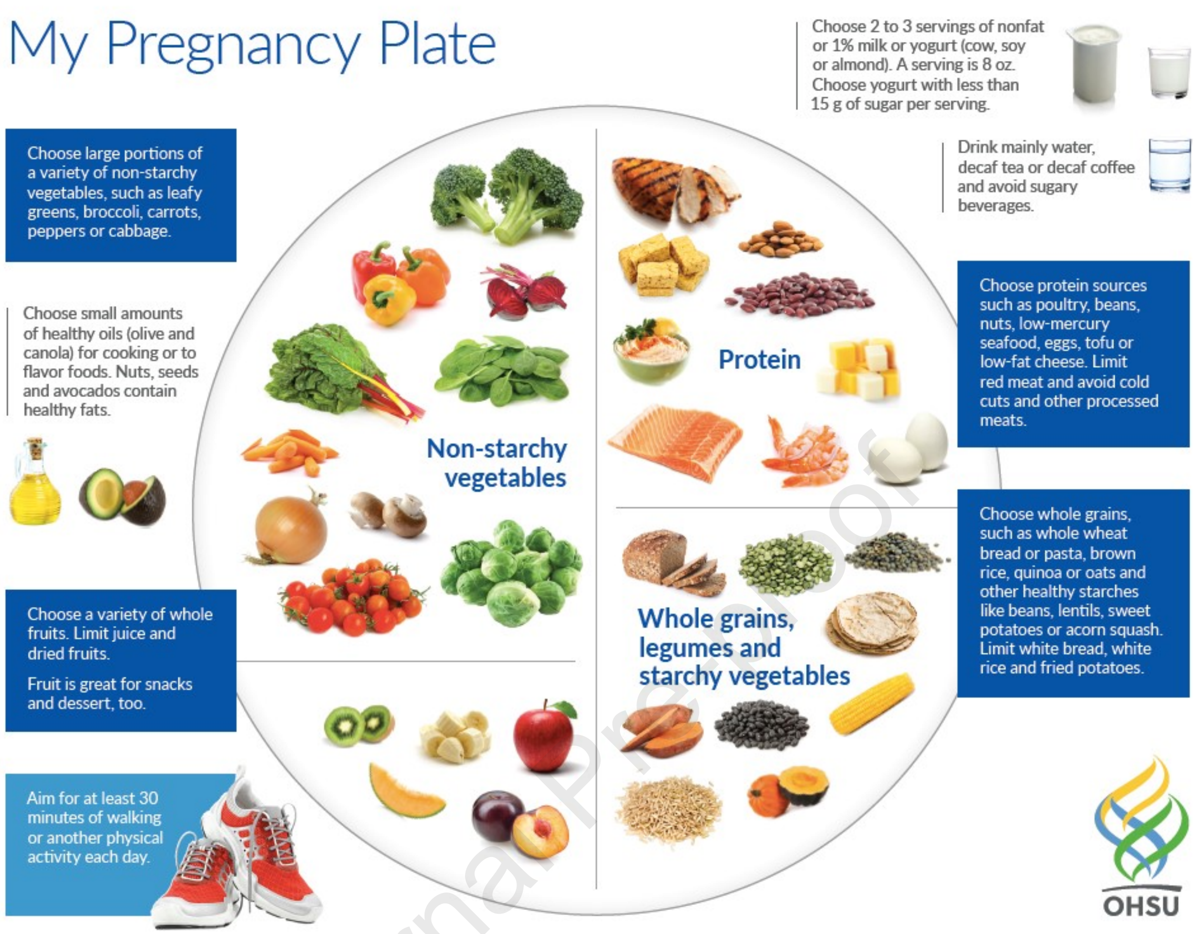
- higher in vegetables; fruits; whole grains; nuts, legumes and seeds; and seafood (preterm birth, only), and
- lower in red and processed meats and fried foods.

Most of the research was conducted in healthy, Caucasian women with access to health care. (Grade: Limited) Evidence is insufficient to estimate the association between dietary patterns before pregnancy and gestational age at birth as well as the risk of preterm birth. (Grade: Grade not assignable)

Birthweight: No conclusion can be drawn on the association between dietary patterns during pregnancy and birth weight outcomes. Although research is available, the ability to draw a conclusion is restricted by

- inconsistency in study findings,
- inadequate adjustment of birth weight for gestational age and sex, and
- variation in study design, dietary assessment methodology, and adjustment of key confounding factors. (Grade: Grade not assignable)

Insufficient evidence exists to estimate the association between dietary patterns before pregnancy and birth weight outcomes. There are not enough studies available to answer this question. (Grade: Grade not assignable)


My Pregnancy Plate
Choose 2 to 3 servings of nonfat or 1% milk or yogurt (cow, soy or almond). A serving is 8 oz. Choose yogurt with less than 15 g of sugar per serving.
Drink mainly water, decaf tea or decaf coffee and avoid sugary beverages.
Choose large portions of a variety of non-starchy vegetables, such as leafy greens, broccoli, carrots, peppers or cabbage.
Choose small amounts of healthy oils (olive and canola) for cooking or to flavor foods. Nuts, seeds and avocados contain healthy fats.
Non-starchy vegetables
Protein
Choose protein sources such as poultry, beans, nuts, low-mercury seafood, eggs, tofu or low-fat cheese. Limit red meat and avoid cold cuts and other processed meats.
Choose whole grains, such as whole wheat bread or pasta, brown rice, quinoa or oats and other healthy starches like beans, lentils, sweet potatoes or acorn squash. Limit white bread, white rice and fried potatoes.
Whole grains, legumes and starchy vegetables
Choose a variety of whole fruits. Limit juice and dried fruits.
Fruit is great for snacks and dessert, too.
Aim for at least 30 minutes of walking or another physical activity each day.
OHSU


This chart can help you choose which fish to eat, and how often to eat them, based on their mercury levels.
What is a serving? As a guide, use the palm of your hand.
For an adult
1 serving = 4 ounces
Eat 2 to 3 servings a week from the "Best Choices" list (OR 1 serving from the "Good Choices" list).
For children, a serving is 1 ounce at age 2 and increases with age to 4 ounces by age 11.
If you eat fish caught by family or friends, check for fish advisories. If there is no advisory, eat only one serving and no other fish that week.*
Best Choices
EAT 2 TO 3 SERVINGS A WEEK
Anchovy
Atlantic croaker
Atlantic mackerel
Black sea bass
Butterfish
Catfish
Clam
Cod
Crab
Crawfish
Flounder
Haddock
Hake
Herring
Lobster, American and spiny
Mullet
Oyster
Pacific chub mackerel
Perch, freshwater and ocean
Pickerel
Plaice
Pollock
Salmon
Sardine
Scallop
Shad
Shrimp
Skate
Smelt
Sole
Squid
Tilapia
Trout, freshwater
Tuna, canned light (includes skipjack)
Whitefish
Whiting
OR
Good Choices
EAT 1 SERVING A WEEK
Bluefish
Buffalofish
Carp
Chilean sea bass/ Patagonian toothfish
Grouper
Halibut
Mahi mahi/ dolphinfish
Monkfish
Rockfish
Sablefish
Sheepshead
Snapper
Spanish mackerel
Striped bass (ocean)
Tilefish (Atlantic Ocean)
Tuna, albacore/ white tuna, canned and fresh/frozen
Tuna, yellowfin
Weakfish/ seatrout
White croaker/ Pacific croaker
Choices to Avoid
HIGHEST MERCURY LEVELS
King mackerel
Marlin
Orange roughy
Shark
Swordfish
Tilefish (Gulf of Mexico)
Tuna, bigeye
* Some fish caught by family and friends, such as larger carp, catfish, trout and perch, are more likely to have fish advisories due to mercury or other contaminants. State advisories will tell you how often you can safely eat those fish.
www.FDA.gov/fishadvice
www.EPA.gov/fishadvice
EPA United States Environmental Protection Agency
FDA U.S. FOOD & DRUG ADMINISTRATION
This advice supports the recommendations of the 2015-2020 Dietary Guidelines for Americans, developed for people 2 years and older, which reflects current science on nutrition to improve public health. The Dietary Guidelines for Americans focuses on dietary patterns and the effects of food and nutrient characteristics on health. For advice about feeding children under 2 years of age, you can consult the American Academy of Pediatrics.
‡ THIS ADVICE REFERS TO FISH AND SHELLFISH COLLECTIVELY AS "FISH" / ADVICE REVISED JULY 2019