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Review

# The importance of maternal nutrition for health

Irene Cetin, Arianna Laoreti

Department of Mother and Child, Hospital Luigi Sacco, University of Milan, Milan, Italy

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*From the womb to the adult*

Guest Editors: Vassilios Fanos (Cagliari, Italy), Michele Mussap (Genoa, Italy), Antonio Del Vecchio (Bari, Italy), Bo Sun (Shanghai, China), Dorret I. Boomsma (Amsterdam, the Netherlands), Gavino Faa (Cagliari, Italy), Antonio Giordano (Philadelphia, USA)

## Abstract

Nutrition plays a major role in maternal and child health and it is widely recognized that optimum nutrition in early life is the foundation for long-term health. A healthy maternal dietary pattern, along with adequate maternal body composition, metabolism and placental nutrient supply, reduces the risk of maternal, fetal and long-term effects in the offspring. While undernutrition is mainly an issue of low-income countries, malnutrition, due to poor quality diet, is becoming a global health problem.

Preconceptional counseling of women of childbearing age should spread awareness of the importance of maternal nutrition before and during pregnancy and should promote a cultural lifestyle change, in favor of a healthy weight before conceiving and balanced healthy diet with high-quality foods consumption. Supplementation and/or fortification can make a contribution when recommended micronutrient intakes are difficult to be met through food alone. In industrialized countries, although a balanced diet is generally accessible, a switch to a high-fat and low-quality diet has led to inadequate vitamin and mineral intake during pregnancy. Evidence do not support a routine multiple micronutrient supplementation but highlights the importance of an individualized approach, in order to recognize nutritional deficiencies of individuals, thus leading to healthful dietary practices prior to conception and eventually to tailored supplementation.

## Keywords

Maternal nutrition, pregnancy outcome, infant outcome, dietary pattern, malnutrition, supplementation.

## Corresponding author

Irene Cetin, Department of Mother and Child, Hospital Luigi Sacco, University of Milano, Italy; email: irene.cetin@unimi.it.

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## Introduction

Pregnancy represents a unique *époque* in life with considerable potential to influence not only maternal health but also the health of the next generation. Nutrition plays a major role in maternal and child health and dietary interventions in pregnancy can influence maternal, fetal and infant health.

Poor maternal nutritional status, along with maternal body composition, metabolism and placental nutrient supply, are the main factors that can negatively or positively influence fetal development and have been strictly related to adverse pregnancy outcome and expression of fetal genetic potential.

Nevertheless, the association between maternal nutrition and birth outcome is quite complex and influenced by different biologic, socioeconomic, and demographic factors, which vary widely in different populations. Understanding the relationship between maternal nutrition, pregnancy and birth outcomes may provide a basis for developing nutritional interventions that will improve birth outcomes and long-life health of the newborn, improving the quality of life and reducing mortality, morbidity, and health-care costs.

## Maternal dietary pattern and pregnancy and infant outcomes

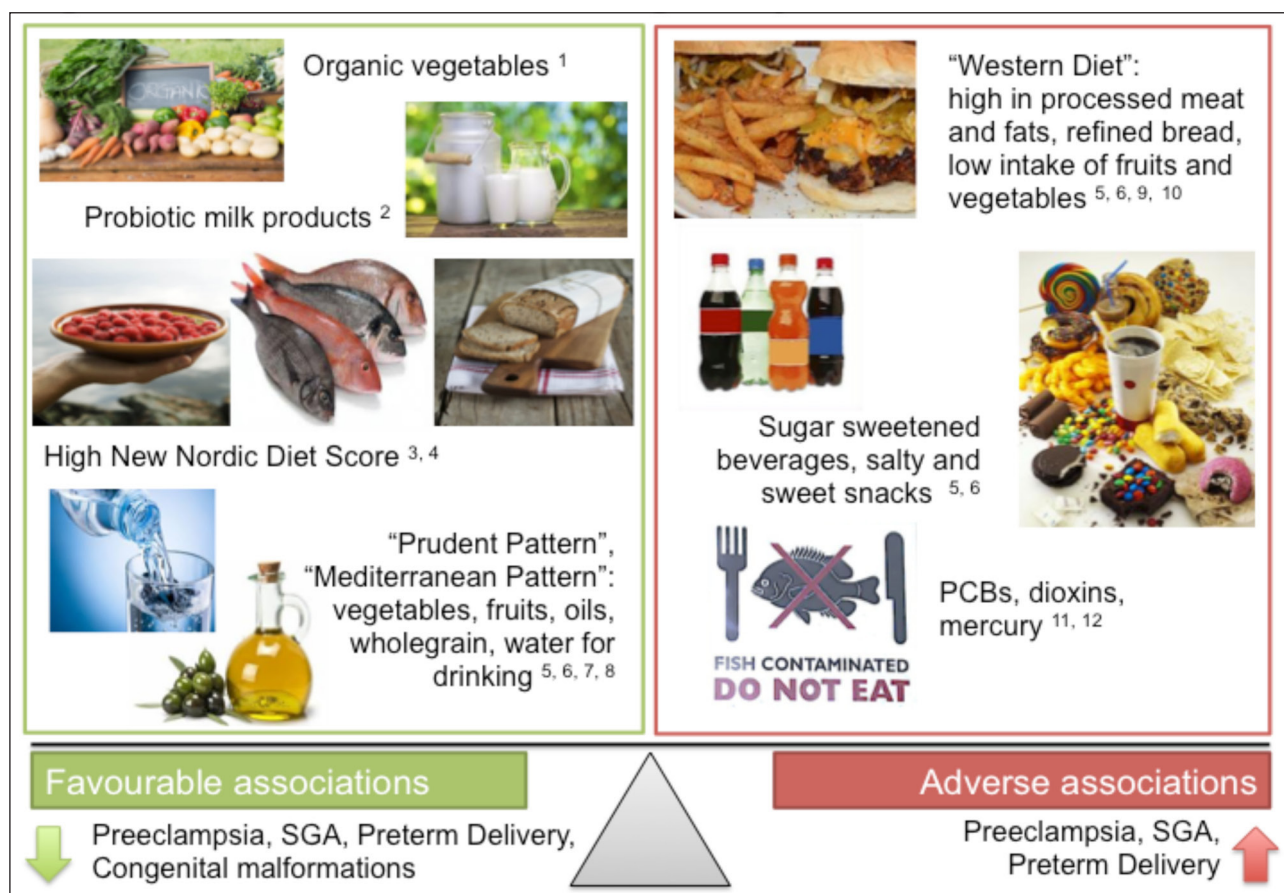
Macro- and micronutrients are direct regulators of DNA stability and phenotypic adaptation, by influencing the availability of methyl donors and mechanisms promoting DNA stability; thereby they serve as substrates, transcription factors and modifiers of gene expression, influencing complex biological pathways involved in embryogenesis, as well as fetal growth and development [1].

A number of studies have investigated the relationship between diet and unfavorable obstetric outcomes. This relationship can be examined at the level of nutrients, foods, or dietary patterns. It is

immediately apparent that identifying the potential influence of single substances is difficult. Nutrients from natural food sources are generally consumed in meals and not as isolated components, so that the usual diet contains thousands of nutrients, while the same substance is present in different foods and foods are not consumed independently of each other. Therefore, the use of dietary patterns, a measure of overall dietary behavior, has become widespread in nutrition research in recent years as an alternative approach to studying individual components of the diet. Dietary patterns research examines the influence of foods eaten in combination and allows for interactions between nutrients, giving a broader and more balanced description of data, and overcoming the methodological limitations related to the study of single nutrients or foods [2, 3].

Dietary patterns are population specific, since they are influenced by sociocultural factors and food availability. They can be characterized on the basis of *a priori* knowledge (hypothesis oriented approach) or by the use of data driven techniques (empirically derived dietary patterns), such as principal component factor analysis (PCA) derived from food frequency questionnaires (FFQs) [4]. To date, dietary patterns have been associated with biomarker concentrations and related to complex diseases, such as cardiovascular disease [5]. Dietary scores in pregnant women have been constructed in a variety of populations, including British [6], Spanish [7], Norwegian [8], and Japanese [9] populations.

Several findings on the association between different maternal dietary patterns and pregnancy and infant outcomes have been recently described from large prospective pregnancy and birth cohorts population studies, such as the Danish National Birth Cohort (DNBC) and the Norwegian Mother and Child Cohort Study (MoBa) [10, 11]. During 1996-2002, 101,042 pregnancies were recruited for the DNBC, and during 1999-2008, 108,000 pregnancies were recruited for the MoBa [10]. Assessing nutritional exposures in pregnancy was a main priority in both cohorts, with approximately 70,183 (74.2% of those who received a food frequency questionnaire [FFQ]) and 87,000 (90.4%) of the pregnant women having completed a FFQ in DNBC and MoBa, respectively. The two cohorts comprise, to date, the largest prospective databases worldwide, holding extensive information on prenatal and early life exposures, in particular maternal diet, and pregnancy outcome and diseases in the offspring. **Fig. 1** summarizes the



**Figure 1.** Maternal diet and pregnancy and infant outcome.

<sup>1</sup>Torjusen et al. 2014 [13], <sup>2</sup>Brantsaeter et al., 2011 [91]; <sup>3</sup>Hillesund et al., 2014 [14]; <sup>4</sup>Brantsaeter et al., 2012 [92]; <sup>5</sup>Englund-Ogge et al., 2014 [15]; <sup>6</sup>Brantsaeter et al., 2009 [12]; <sup>7</sup>Vujkovic et al., 2009 [22]; <sup>8</sup>Thompson et al., 2010 [21]; <sup>9</sup>Rasmussen et al., 2014 [16]; <sup>10</sup>Chatzi et al., 2013 [24]; <sup>11</sup>Papadopoulou et al., 2013 [93]; <sup>12</sup>Vejrup et al., 2014 [94].

main results for the investigated dietary patterns of cohorts' population studies.

Data derived from the MoBa cohort demonstrated that women with high scores on a pattern characterized by high intake of vegetables, plant foods, and vegetable oils were at decreased risk of preeclampsia, whereas a dietary pattern characterized by high consumption of processed meat, sweet drinks, and salty snacks increased the risk [12].

At the same time, another recent publication from the MoBa presented evidence that pregnant women who often eat organic vegetables have a lower risk of preeclampsia than women who rarely or never do (crude OR = 0.76, 95% CI 0.61 to 0.96; adjusted OR = 0.79, 95% CI 0.62 to 0.99), even after adjusting for overall dietary quality [13]. Possible explanations for an association between preeclampsia and use of organic vegetables could be that organic vegetables may change the exposure to pesticides, secondary plant metabolites and may influence the composition of the gut microbiota.

Similarly, a great adherence to the New Nordic Diet, based on consumption of Nordic fruits, root vegetables, cabbages, potatoes, oatmeal porridge, whole grains, wild fish, game, berries, milk and water, was associated with a lower risk of developing preeclampsia and spontaneous preterm delivery among nulliparous women [14].

Moreover, it has been recently demonstrated that pregnant women from the same cohort, with high scores on the "prudent" dietary pattern (based on raw and cooked vegetables, salad, onion, garlic, fruit and berries, nuts, vegetable oils, water as beverage, whole grain cereals, poultry, and fiber rich bread) have a reduced risk of preterm delivery (0.88, 95% CI 0.80 to 0.97) [15].

Similarly, a recent study from the DNBC reported that Western-type diet, high in meat and fats and low in fruits and vegetables, is associated with increased odds of induced preterm birth [16].

Many studies have also specifically evaluated the importance of fish consumption for the prevention of preterm delivery and for other

pregnancy outcomes [17]. Fish is of particular importance for the content in long-chain  $\omega$ -3 fatty acids like DHA. However, due to potential presence of contaminants such as mercury and dioxins, the advice is to eat fish on average 2 times per week avoiding fish with higher contaminant levels such as tuna and sword fish [18].

As regards to fetal and neonatal outcome, several studies found an association with different maternal dietary patterns. A study by Wolff conducted in Mexican American pregnant women found that an eating pattern characterized by fats, oils, breads, cereals, high fat meats, sugar, etc. was associated with decreased birthweight [19]. In line with these results, a study by Okubo conducted in the Japanese population and a study by Thompson conducted in New Zealand confirmed that adherence to a “traditional” diet, poor in confectioneries, soft drinks and junk food, decreased the risk of having a small for gestational age (SGA) infant [20, 21]. Moreover, a predominantly “Mediterranean” dietary pattern characterized by joint intakes of fruit, vegetables, vegetable oil, alcohol, fish, legumes and cereals and low intakes of potatoes and sweets has been associated with a decreased risk of spina bifida in the offspring. In this study, the Mediterranean dietary pattern was correlated with higher levels of serum folate, serum vitamin B12 and lower plasma homocysteine [22]. In addition, a healthy maternal dietary pattern has been recently associated to positive long-term effects, such as increased child bone mass [23], reduced child asthma [24] and pediatric tumors [25].

It is therefore well recognized that unhealthy maternal diet significantly contributes to impaired pregnancy and offspring outcomes. It is likely that dietary patterns with better micronutrient intakes (green leafy vegetables, fruits, whole-grain breads/cereals, oily fish, eggs) positively influence placental development, thus decreasing the risk of developing pathologies related to abnormal placentation, such as preeclampsia and to an abnormal maternal-placental interface, like premature delivery [1].

Unfortunately, most women do not get enough micronutrients in their diet during reproductive age, as well as during pregnancy, representing an important topic of public health not only in developing countries but also in industrialized countries where dietary patterns, typified by snacking, breakfast skipping, fast foods, soft drinks and convenience foods, are nutritionally unbalanced and fail to meet recommended daily allowance for micronutrients [26-28]. This situation

is further exacerbated by the reduction of minerals, vitamins, and protein in fruits and vegetables due to environmental/dilution effects [29].

## Maternal anthropometrics and nutritional status

### *Body mass index and gestational weight gain*

Maternal body mass index (BMI) and gestational weight gain (GWG) represent the major determinants of maternal adaptation to incremental energy needs during pregnancy. Several findings support the evidence that anthropometric indicators of nutritional status, like maternal pre-pregnancy BMI and GWG, are critical predictors of maternal and fetal short- and long-term outcomes [30]. Optimizing pre-pregnancy BMI together with appropriate counseling during pregnancy to obtain adequate GWG, should be considered a priority by health care systems and providers, in order to reduce pregnancy and infant associated adverse outcomes [31, 32].

Data from the World Health Organization (WHO) Collaborative Study on Maternal Anthropometry and Pregnancy Outcomes on 110,000 births from 20 different countries were used to define anthropometric indicators which are most predictive of fetal outcome (birthweight and preterm birth) and maternal outcome (preeclampsia, post partum hemorrhage and assisted delivery) [33]. Birthweights between 3,100 and 3,600 g (mean 3,300) g were associated with a lower risk of fetal and maternal complications. The range of GWG associated with birthweight > 3,000 g was 10-14 (mean 12) kg.

Because of the interaction between pre-pregnancy BMI and GWG on pregnancy and fetal outcome, the Institute of Medicine (IOM) recommended different ranges of GWG for women with low, normal and high BMI [34]. Both high and low GWG have been associated with adverse pregnancy and fetal outcomes, even in women with a normal pre-pregnancy BMI. Evidence supports association between excessive GWG and increased birthweight, caesarean delivery rate and postpartum weight retention (with subsequent obesity and long-term comorbidity associated) [34]. On the other hand, many epidemiologic studies are consistent in showing a linear, direct relationship between lower GWG and decreased birthweight [35]. Relative risks for GWG and small for gestational age (SGA) appear to be higher among women with lower pre-pregnancy BMI.



Moreover, low GWG is moderately associated with failure to initiate breastfeeding [31, 34].

A recent study analyzed the effect of maternal anthropometrics on neonatal lean and fat mass, as well as possible sex-specific differences [36]. In male infants, but not in female, maternal height, body mass index and weight gain were significant predictors of both lean and fat mass, suggesting that the body composition and inflammatory environment of the mother modulate the metabolic fitness of neonates, as predicted by fat and lean mass. The only measured maternal factors that predicted female body composition were markers of inflammation (plasma C-reactive protein and interleukin-6). Maternal weight gain and pre-pregnancy anthropometrics were equally predictive of male fetal growth when placental weight and gestational age were accounted for [36]. This finding contradicts the idea that pre-pregnancy nutrition is of greater importance than weight gain during pregnancy [37, 38]. Authors commented that both long- and short-term nutritional indicators are key influences on fetal fat, lean mass growth, and adiposity in a sex-specific manner.

#### *Maternal malnutrition*

Maternal malnutrition can result, primarily, from a diet that does not allow an adequate caloric intake, resulting in undernutrition or overnutrition and secondary, but not least important, it may also follow from a diet based on poor quality nutrients with reduced amounts of micronutrients. Each of these conditions may have profound impact on pregnancy and infant outcomes [39].

#### **Maternal undernutrition**

Several animal studies examined the effects of restricting total caloric intake or reducing dietary protein content on fetoplacental development. Maternal undernutrition may potentially alter fetal growth trajectory by modifying placental weight, surface and nutrient transfer capacity, depending on the severity of the nutritional challenge and on the time of deprivation, as documented by the Dutch famine during the Second World War. Undernutrition during mid or late gestation reduced placental length and area and was associated with smaller babies due to a reduced placental efficiency. Babies in early gestation during the famine, or conceived

after the famine end, had higher birthweights suggesting increased placental efficiency due to compensatory mechanisms (increased placental mass, surface and transport) [40-42]. Moreover, exposure to undernutrition during any stage of gestation was associated with higher risk of later glucose intolerance. Interestingly, exposure only during early gestation increased risk of obesity, coronary heart disease, schizophrenia and depression [40], suggesting that early gestation is a pregnancy vulnerable period but also that pre- and peri-conceptual nutrition may have negative consequences for the offspring's health, probably based on abnormal placentation occurring early in pregnancy. A recent study in an ovine model found that maternal undernutrition throughout pregnancy may have adverse effects on developing fetal appetitive pathways, increasing orexigenic gene expression in the late gestation fetal hypothalamus, contributing to programmed hyperphagia and obesity in intrauterine growth-restricted, low birthweight offspring [43].

Furthermore, excessive exposure to endogenous glucocorticoids in utero, caused by maternal undernutrition, affects placental development and nutrient carriers expression determining intrauterine growth restriction (IUGR) [44]. In animal models, maternal undernutrition during peri-conceptual and gestational periods alters the insulin-like growth factor (IGF) system in the fetus leading to compromised fetal growth [45]. A meta-analysis by Imdad in 2012 reported that a balanced protein-energy supplementation is an effective intervention to reduce the risk of LBW and SGA births in undernourished women of developing countries [46].

In addition to these findings, pre-pregnancy underweight has been associated with increased risk of preterm birth, reported as an additional risk of 32% in a recent meta-analysis (RR 1.32, 95% CI 1.22-1.43) [30, 47, 48].

Adolescent girls who are still growing at the time of conception represent a specific vulnerable group at higher risk of undernutrition during pregnancy. Animal studies have been conducted in ovine prevented from growing during pregnancy by relative underfeeding. It has been demonstrated that limiting maternal intake gradually depletes maternal body reserves leading to a lower transplacental glucose gradient and a modest slowing of fetal growth in late pregnancy. These changes appear to be independent of alterations in placental growth *per se* [49].

**Maternal overnutrition: overweight and obese women**

With the “epidemic” increase of over-weight and obese women, overnutrition is emerging as a major health problem worldwide, with obesity affecting an estimated 500 million people [50, 51]. Among women of childbearing age, up to three in ten are obese [52, 53], defined as having a body mass index (BMI) greater than or equal to 30 kg/m<sup>2</sup>, 10% of whom meet the criteria for obesity class II (BMI: 35-39.9 kg/m<sup>2</sup>) or III (BMI: ≥ 40 kg/m<sup>2</sup>) [53].

Pre-pregnancy obesity has been associated with both short- and long-term pregnancy complications for both mothers and offspring. Pre-pregnancy obesity has been linked to increased risk of hypertensive disorders of pregnancy [54, 55], gestational diabetes mellitus [56], as well as an entire spectrum of adverse pregnancy outcomes, including increased risk of caesarean delivery [57], poor lactation practices [58], obstetric anesthesia-related complications, prolonged gestation, maternal infectious morbidity and decreased success with trial of labor [30]. In addition, maternal obesity is a cause for stillbirths, fetal and neonatal death [59, 60], abnormal fetal growth with large for gestational age infants [61] or fetal growth restriction, preterm birth [62] and increased risk of a range of structural anomalies [63].

The placental to fetal weight ratio has been shown to be increased in obese pregnancies, suggesting that placentas of obese women are less efficient, with gender specific responses [64]. Similar changes in placental biometric parameters have been associated with increased risks of cardiovascular disease in later life [65]. More in detail, obesity induces a chronic, low-grade intrauterine inflammation with over-expression of maternal C-reactive protein determining a pathological fetal state, compromising placental function and metabolism and altering fetal growth and development [66, 67]. Interestingly, obese mothers who lose weight during pregnancy have an increased risk of SGA [68, 69]. This could be possibly explained by a number of mechanisms, such as ketosis resulting from the mobilization of white fat stores and partial oxidation of fatty acids in the liver, deficiencies of nutrients in the fetus because of increased utilization by maternal tissues, and elevations of cortisol that inhibit fetal protein synthesis.

As mentioned before, maternal obesity has also been associated with long-term health consequences for the offspring. Maternal obesity perpetuates the obesity epidemic, since children of obese women

are more likely to be obese themselves and to suffer from chronic cardiovascular diseases [70, 71] starting from young age. More in detail, maternal obesity in early pregnancy has been associated with a four- and two-fold increased risk of childhood overweight and obesity [72], respectively, likely through genetic as well as pre- and postnatal environmental factors. Childhood overweight is a strong predictor of adult obesity [73]. Of note, overweight/obese women with normal glucose tolerance levels have neonates with increased fat mass compared to lean/average weight women [74]. Breastfeeding seems to reduce the magnitude of risk of being overweight during childhood in children from obese mothers [75]. The characterization of human breast milk and formula milk metabolome and, contextually, of neonate metabolism can synergistically contribute to assess how single nutrients influence the metabolic regulation in infant and to formulate dietary intervention aimed at meeting the needs of newborn [76]. A recent study supported the hypothesis that the combination of maternal obesity in early pregnancy and high protein intake in infant formula feeding might predispose to obesity risk in later life [77]. Authors conducted metabolomics analysis on infants’ stool and urine of obese women finding that formula-fed infants were metabolically different from breast-fed infants, at the level of lipid and energy metabolism (carnitines, ketone bodies, and Krebs cycle) [77].

Minimizing the overall risks associated with maternal obesity represents a public health priority. Given that weight is a modifiable risk factor, research should be directed on how healthcare interventions and public health campaigns can reduce these risks.

**Micronutrients deficiency: maternal poor quality nutrition**

A healthy diet must be balanced not only in terms of macronutrients content (intake of proteins, carbohydrates and fats), but also in terms of micronutrients intake (vitamins and mineral), for which we may more easily incur into deficiencies or inadequacies.

Imbalances of micronutrients before and during pregnancy can negatively influence both mother and fetus with significantly high reproductive risks, ranging from infertility to fetal structural defects, abnormal fetal development and growth and long-term diseases [26, 78, 79].

On the other side, healthy dietary patterns and micronutrients supplementation, particularly during the peri-conceptional period, are related

to improved birth outcomes, probably through alterations in maternal and fetal metabolism due to micronutrients role/involvement in enzymes, signal transduction, transcription pathways, oxidative stress and epigenetic modifications [26]. Since different pregnancy stages represent a continuum, from the pre-conception to the post-partum period, an injury acting before conception or in early pregnancy may have long-lasting effects on the well-being of the mother and the fetus, and may further influence the health of the baby at a later age, by programming postnatal pathophysiology. Each stage of fetal development is dependent on and influenced by appropriate maternal nutrient supply; the timing of nutritional insults impacts differently on the nature of adult diseases. The period from conception to implantation is particularly important for fetal growth and development [26, 80].

Undernourished women are at particular risk of micronutrient deficiency. Nevertheless, inadequacy of micronutrients intake is also typical of obese “western” diets, poor of vegetables and fruit. Indeed, over-nourished women are often mal-nourished, with macro- and/or micronutrients imbalances potentially affecting fetal growth [81]. Recent studies demonstrate that obese women transfer less 25-hydroxyvitamin D (25-OH-D) to the fetus than normal-weight women (with cord blood 25-OH-D levels directly correlating to neonatal percentage body fat) [82] and present lower maternal serum folate concentrations which is a rate-limiting factor for placental folate transport to the fetus [83].

### Healthy diet and supplementation needs

Several studies support the evidence that the frequency and severity of pregnancy complications may be reduced through an improvement in the macro- and, especially, micronutrient status of the mothers.

The optimal mode of meeting recommended micronutrient intakes is to ensure consumption of a balanced diet that is adequate in every nutrient [28, 84]. Unfortunately, this is far from being achievable everywhere, since it requires universal access to adequate food and appropriate dietary habits.

Worldwide micronutrient intakes do not fit pregnancy requirements, so that their supplementation is recommended from the beginning of pregnancy in most of the low- and middle-income countries in order to avoid deficiencies and adverse pregnancy outcomes. A recent meta-analysis of 21 randomized controlled

trials on the effects of multiple supplementation on pregnancy outcome found that, in low-/middle-income countries, women who received multiple supplements had a significant reduction in the risk of SGA offspring compared with women who received iron/folate supplements alone (RR 0.87, 95% CI 0.81-0.95) [85].

However, contrary to previous thinking, micronutrient malnutrition is not uniquely a concern of low-income countries [86]. Despite the availability of economic and nutritional resources, in the last decades the switch to a high-fat and low-quality diet, together with smoking habits, stress, as well as infectious and genetic factors, has led to a low micronutrient intake and to nutritional deficiencies even in developed countries, as documented by recent studies.

In a recent meta-analysis of 62 studies (n = 108,733 subjects), Blumfield et al. [27] analyzed micronutrient intakes in pregnant women in the USA (19 studies, n = 5,994), Canada (2 studies, n = 95), the UK (16 studies, n = 15,404), Europe (16 studies, n = 85,071), Australia (2 studies, n = 632), New Zealand (2 studies, n = 291) and Japan (5 studies, n = 1,249). Data from this study revealed folate, iron and vitamin D intakes consistently below national nutrient recommendations in each geographical region, while calcium intakes were below the national recommendation in all countries studied with the exception of Europe. In particular, despite folate recommendations varying across geographical regions, average folate intakes in all regions were between 13% and 63% lower than recommendations. Similarly, iron intakes reported by pregnant women were below nutrient recommendations in almost all developed regions. The importance of iron and folate intakes has also been well recognized in recent evaluations of the EU EURRECA project [87, 88].

In the light of this, supplementation and/or fortification can make a contribution when the high demands for fetal growth and development are difficult to be met through food alone. In general, studies show that multiple micronutrients supplementation improves outcomes as far as low birthweight, preterm delivery and preeclampsia. A recent Danish study showed a significant reduction of SGA infants in multivitamin users, with the strongest association in regular users from 12 weeks during the peri-conceptional period [89].

Given the high prevalence of multiple micronutrient deficiencies in low-to-middle-income countries, the challenge is to implement

intervention strategies that combine appropriate maternal and child health interventions (education, dietary modification, food provision, agricultural interventions) with micronutrient interventions [84].

As regards to developed countries, currently there is insufficient evidence to support routine supplementation at the population level, except for peri-conceptual folate supplementation. In the USA, the IOM and the Center for Disease Control and Prevention (CDC) recommend multivitamin supplements for pregnant women who do not consume an adequate diet [90]. Nutritional counseling for women of reproductive age should be a public health priority. Many women are still unaware of how much their nutritional status impacts their pregnancy and infant outcomes, and improving women's nutrition and weight-related behaviors should therefore begin during their earlier reproductive years. Dietary recommendations for women of childbearing age should promote greater consumption of green leafy vegetables, whole-grain breads/cereals, oily fish, eggs, and fortified food products. Furthermore each woman, who does not avoid a pregnancy, should be advised to use folic acid supplements during the peri-conceptual period.

In addition, in order to avoid nutritional deficiencies and to encourage women to establish healthful dietary practices prior to conception, an individualized approach should be considered for each woman, taking into account the phenotypic, genotypic and metabolic differences among individuals of the same population.

In general, there is growing interest in multiple micronutrient supplementation in "at-risk" populations in whom multiple deficiencies often coexist. The recognition of these particular subgroups of population (e.g. low socioeconomic status, obesity, previous bariatric surgery, underweight, heavy smokers, substance abusers, adolescence, short inter-pregnancy interval, vegetarian or vegan diet, multiple gestation, celiac disease and specific pregnancy risks) is of paramount importance, in order to early detect inadequate intakes, promote healthful dietary practices prior to conception and eventually individualize supplementation based on specific needs.

## Conclusions

Evidence derived from studies investigating both macro- and micronutrients intake, clearly suggests that maternal nutrition is able to influence individual

health even before birth. A healthy maternal dietary pattern, during the peri-conceptual period and throughout pregnancy, reduces the risk of maternal and infant complications, as well as long-life consequences. Dietary patterns with better micronutrient intakes (green leafy vegetables, fruits, whole-grain breads/cereals, oily fish etc.) positively influence the formation of a normal placenta at the beginning of pregnancy, fundamental later on in the developing fetus, thus decreasing the risk preeclampsia, premature delivery and abnormal fetal growth. While undernutrition is mainly an issue of developing countries, malnutrition, due to poor quality diet, is becoming a global problem.

Spreading the awareness of the importance of maternal nutrition before and during pregnancy and stimulating a cultural change in favor of a balanced healthy diet and high-quality foods consumption, is necessary for improving future global health.

## Declaration of interest

The Authors declare that there is no conflict of interest.

## References

1. Cetin I, Mandò C, Calabrese S. Maternal predictors of intrauterine growth restriction. *Curr Opin Clin Nutr Metab Care*. 2013;16(3):310-9.
2. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002;13:3-9.
3. Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr*. 2001;73:1-2.
4. Newby PK, Tucker KL. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev*. 2004;62:177-203.
5. Weikert C, Hoffmann K, Dierkes J, Zyriax BC, Klipstein-Grobusch K, Schulze MB, Jung R, Windler E, Boeing H. A homocysteine metabolism-related dietary pattern and the risk of coronary heart disease in two independent German study populations. *J Nutr*. 2005;135:1981-8.
6. Northstone K, Emmett PM. A comparison of methods to assess changes in dietary patterns from pregnancy to 4 years postpartum obtained using principal components analysis. *Br J Nutr*. 2008;99:1099-106.
7. Cuco G, Fernández-Ballart J, Sala J, Viladrich C, Iranzo R, Vila J, Arija V. Dietary patterns and associated lifestyles in preconception, pregnancy and postpartum. *Eur J Clin Nutr*. 2006;60:364-71.
8. Torjusen H, Lieblein G, Naes T, Haugen M, Meltzer HM, Brantsæter AL. Food patterns and dietary quality associated with organic food consumption during pregnancy; data from a large cohort of pregnant women in Norway. *BMC Public Health*. 2012;12:612.



9. Okubo H, Miyake Y, Sasaki S, Tanaka K, Murakami K, Hirota Y; Osaka Maternal and Child Health Study Group. Nutritional adequacy of three dietary patterns defined by cluster analysis in 997 pregnant Japanese women: the Osaka Maternal and Child Health Study. *Public Health Nutr.* 2011;14:611-21.
10. Meltzer HM, Brantsaeter AL, Nilsen RM, Magnus P, Alexander J, Haugen M. Effect of dietary factors in pregnancy on risk of pregnancy complications: results from the Norwegian Mother and Child Cohort Study. *Am J Clin Nutr.* 2011;94(6 Suppl):1970-4S.
11. Magnus P, Irgens LM, Haug K, Nystad W, Skjaerven R, Stoltenberg C. Cohort profile: the Norwegian Mother and Child Cohort Study (MoBa). *Int J Epidemiol.* 2006;35:1146-50.
12. Brantsaeter AL, Haugen M, Samuelsen SO, Torjusen H, Trogstad L, Alexander J, Magnus P, Meltzer HM. A dietary pattern characterized by high intake of vegetables, fruits, and vegetable oils is associated with reduced risk of preeclampsia in nulliparous pregnant Norwegian women. *J Nutr.* 2009;139:1162-8.
13. Torjusen H, Brantsaeter AL, Haugen M, Alexander J, Bakketeig LS, Lieblein G, Stigum H, Næs T, Swartz J, Holmboe-Ottesen G, Roos G, Meltzer HM. Reduced risk of pre-eclampsia with organic vegetable consumption: results from the prospective Norwegian Mother and Child Cohort Study. *BMJ Open.* 2014;4(9):e006143.
14. Hillesund ER, Øverby NC, Engel SM, Klungsøy K, Harmon QE, Haugen M, Bere E. Associations of adherence to the New Nordic Diet with risk of preeclampsia and preterm delivery in the Norwegian Mother and Child Cohort Study (MoBa). *Eur J Epidemiol.* 2014;29(10):753-65.
15. Englund-Ögge L, Brantsaeter AL, Sengpiel V, Haugen M, Birgisdottir BE, Myhre R, Meltzer HM, Jacobsson B. Maternal dietary patterns and preterm delivery: results from large prospective cohort study. *BMJ.* 2014;348:g1446.
16. Rasmussen MA, Maslova E, Halldorsson TI, Olsen SF. Characterization of dietary patterns in the Danish national birth cohort in relation to preterm birth. *PLoS One.* 2014;9(4):e93644.
17. Cetin I, Koletzko B. Long-chain omega-3 fatty acid supply in pregnancy and lactation. *Curr Opin Clin Nutr Metab Care.* 2008;11(3):297-302.
18. Koletzko B, Cetin I, Brenna JT for Perinatal Lipid Intake Working Group. Dietary fat intakes for pregnant and lactating women. *Br J Nutr.* 2007;98(5):873-7.
19. Wolff CB, Wolff HK. Maternal eating patterns and birth weight of Mexican American infants. *Nutr Health.* 1995;10:121-34.
20. Okubo H, Miyake Y, Sasaki S, Tanaka K, Murakami K, Hirota Y; Osaka Maternal and Child Health Study Group, Kanzaki H, Kitada M, Horikoshi Y, Ishiko O, Nakai Y, Nishio J, Yamamasu S, Yasuda J, Kawai S, Yanagihara K, Wakuda K, Kawashima T, Narimoto K, Iwasa Y, Orino K, Tsunetoh I, Yoshida J, Iito J, Kaneko T, Kamiya T, Kuribayashi H, Taniguchi T, Takemura H, Morimoto Y, Matsunaga I, Oda H, Ohya Y. Maternal dietary patterns in pregnancy and fetal growth in Japan: the Osaka Maternal and Child Health Study. *Br J Nutr.* 2012;107:1526-33.
21. Thompson JM, Wall C, Becroft DM, Robinson E, Wild CJ, Mitchell EA. Maternal dietary patterns in pregnancy and the association with small-for-gestational-age infants. *Br J Nutr.* 2010;103(11):1665-73.
22. Vujkovic M, Steegers EA, Looman CW, Ocké MC, van der Spek PJ, Steegers-Theunissen RP. The maternal Mediterranean dietary pattern is associated with a reduced risk of spina bifida in the offspring. *BJOG.* 2009;116:408-15.
23. Cole ZA, Gale CR, Javaid MK, Robinson SM, Law C, Boucher BJ, Crozier SR, Godfrey KM, Dennison EM, Cooper C. Maternal dietary patterns during pregnancy and childhood bone mass: a longitudinal study. *J Bone Miner Res.* 2009;24(4):663-8.
24. Chatzi L, Apostolaki G, Bibakis I, Skypala I, Bibaki-Liakou V. Protective effect of fruits, vegetables and the Mediterranean diet on asthma and allergies among children in Crete. *Thorax.* 2007;62:677-83.
25. Musselman JR, Jurek AM, Johnson KJ, Linabery AM, Robison LL, Shu XO, Ross JA. Maternal dietary patterns during early pregnancy and the odds of childhood germ cell tumors: A Children's Oncology Group study. *Am J Epidemiol.* 2011;173:282-91.
26. Cetin I, Berti C, Calabrese S. Role of micronutrients in the periconceptional period. *Hum Reprod Update.* 2010;16(1):80-95.
27. Blumfield ML, Hure AJ, Macdonald-Wicks L, Smith R, Collins CE. A systematic review and meta-analysis of micronutrient intakes during pregnancy in developed countries. *Nutr Rev.* 2013;71:118-132.s.
28. Parisi F, Laoreti A, Cetin I. Multiple micronutrient needs in pregnancy in industrialized countries. *Ann Nutr Metab.* 2014;65:13-21.
29. Tilman, D and Clark M. Global diets link environmental sustainability and human health. *Nature.* 2014;515(7528):518-22.
30. Dean SV, Lassi ZS, Imam AM, Bhutta ZA. Preconception care: nutritional risks and interventions. *Reprod Health.* 2014;11(Suppl 3):S3.
31. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines; Rasmussen KM, Yaktine AL (Eds.). *Weight Gain During Pregnancy: Reexamining the Guidelines.* Washington (DC): National Academies Press (US), 2009.
32. Tanentsapf I, Heitmann BL, Adegboye AR. Systematic review of clinical trials on dietary interventions to prevent excessive weight gain during pregnancy among normal weight, overweight and obese women. *BMC Pregnancy Childbirth.* 2011;11:81.
33. A WHO Collaborative Study. Maternal anthropometry and pregnancy outcomes. *Bull World Health Organ.* 1995;73(Suppl):1-98.
34. Siega-Riz AM, Viswanathan M, Moos MK, Deierlein A, Mumford S, Knaack J, Thieda P, Lux LJ, Lohr KN. A systematic review of outcomes of maternal weight gain according to Institute of medicine recommendations: birthweight, fetal growth, and postpartum weight retention. *Am J Obstet Gynecol.* 2009;201:339.e1.
35. Viswanathan M, Siega-Riz AM, Moos MK, Deierlein A, Mumford S, Knaack J, Thieda P, Lux LJ, Lohr KN. Outcomes of maternal weight gain. *Evid Rep Technol Assess.* 2008;(168):1-223.

36. O'Tierney-Ginn P, Presley L, Minium J, Hauguel deMouzon S, Catalano PM. Sex-specific effects of maternal anthropometrics on body composition at birth. *Am J Obstet Gynecol.* 2014;211(3):292.e1-9.
37. Catalano PM. Obesity and pregnancy: the propagation of a viscous cycle? *J Clin Endocrinol Metab.* 2003;88:3505-6.
38. Sanin Aguirre LH, Reza-Lopez S, Levario-Carrillo M. Relation between maternal body composition and birth weight. *Biol Neonate.* 2004;86:55-62.
39. Berti C, Cetin I, Agostoni C, Desoye G, Devlieger R, Emmett PM, Ensenauer R, Hauner H, Herrera E, Hoesli I, Krauss-Etschmann S, Olsen SF, Schaefer-Graf U, Schiessl B, Symonds ME, Koletzko B. Pregnancy and infants' outcome: nutritional and metabolic implications. *Crit Rev Food Sci Nutr.* 2014 Mar 14. [Epub ahead of print].
40. Roseboom T, de Rooij S, Painter R. The Dutch famine and its long-term consequences for adult health. *Early Hum Dev.* 2006;82(8):485-91.
41. Roseboom TJ, Painter RC, de Rooij SR, van Abeelen AF, Veenendaal MV, Osmond C, Barker DJ. Effects of famine on placental size and efficiency. *Placenta.* 2011;32(5):395-9.
42. Vaughan OR, Sferruzzi-Perri AN, Coan PM, Fowden AL. Environmental regulation of placental phenotype: implications for fetal growth. *Reprod Fertil Dev.* 2012;24:80-96.
43. Adam CL, Williams PA, Milne JS, Aitken RP, Wallace JM. Orexigenic Gene Expression in Late Gestation Ovine Fetal Hypothalamus is Sensitive to Maternal Undernutrition and Realimentation. *J Neuroendocrinol.* 2015 Jul 27. [Epub ahead of print].
44. Belkacemi L, Jelks A, Chen CH, Ross MG, Desai M. Altered placental development in undernourished rats: role of maternal glucocorticoids. *Reprod Biol Endocrinol.* 2011;9:105.
45. Igwebuike UM. Impact of maternal nutrition on ovine foetoplacental development: A review of the role of insulin-like growth factors. *Anim Reprod Sci.* 2010;121(3-4):189-96.
46. Imdad A, Bhutta ZA. Maternal nutrition and birth outcomes: effect of balanced protein-energy supplementation. *Paediatr Perinat Epidemiol.* 2012;26(Suppl 1):178-90.
47. Ronnenberg AG, Wang X, Xing H, Chen C, Chen D, Guang W, Guang A, Wang L, Ryan L, Xu X. Low preconception body mass index is associated with birth outcome in a prospective cohort of Chinese women. *J Nutr.* 2003;133(11):3449.
48. Salihi HM, Mbah AK, Alio AP, Clayton HB, Lynch O. Low pre-pregnancy body mass index and risk of medically indicated versus spontaneous preterm singleton birth. *Eur J Obstet Gynecol Reprod Biol.* 2009;144(2):119-23.
49. Wallace JM, Luther JS, Milne JS, Aitken RP, Redmer DA, Reynolds LP, Hay WW Jr. Nutritional modulation of adolescent pregnancy outcome, a review. *Placenta.* 2006;27(Suppl A): S61-8.
50. World Health Organization. Obesity and Overweight. Available at: <http://www.who.int/mediacentre/factsheets/fs311/en/>, last access: August 2015.
51. McKnight JR, Satterfield MC, Li X, Gao H, Wang J, Li D, Wu G. Obesity in pregnancy: problems and potential solutions. *Front Biosci (Elite Ed).* 2011;3:442-52.
52. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA.* 2006;295(13):1549-55.
53. Vahratian A. Prevalence of overweight and obesity among women of childbearing age: results from the 2002 National Survey of Family Growth. *Matern Child Health J.* 2009;13(2):268-73.
54. O'Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of preeclampsia: a systematic overview. *Epidemiology.* 2003;14(3):368-74.
55. Samuels-Kalow ME, Funai EF, Buhimschi C, Norwitz E, Perrin M, Calderon- Margalit R, Deutsch L, Paltiel O, Friedlander Y, Manor O. Prepregnancy body mass index, hypertensive disorders of pregnancy, and long-term maternal mortality. *Am J Obstet Gynecol.* 2007;197(5):490.
56. Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, Dietz PM. Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care.* 2007;30(8):2070-6.
57. Poobalan AS, Aucott LS, Gurung T, Smith WC, Bhattacharya S. Obesity as an independent risk factor for elective and emergency caesarean delivery in nulliparous women – systematic review and meta-analysis of cohort studies. *Obes Rev.* 2009;10(1):28-35.
58. Li R, Jewell S, Grummer-Strawn L. Maternal obesity and breastfeeding practices. *Am J Clin Nutr.* 2003;77(4):931.
59. Nohr EA, Bech BH, Davies MJ, Frydenberg M, Henriksen TB, Olsen J. Prepregnancy obesity and fetal death: a study within the Danish National Birth Cohort. *Obstet Gynecol Survey.* 2005;61(1):7.
60. Kristensen J, Vestergaard M, Wisborg K, Kesmodel U, Secher NJ. Pre-pregnancy weight and the risk of stillbirth and neonatal death. *BJOG.* 2005;112(4):403-8.
61. Black MH, Sacks DA, Xiang AH, Lawrence JM. The relative contribution of prepregnancy overweight and obesity, gestational weight gain, and IADPSG-defined gestational diabetes mellitus to fetal overgrowth. *Diabetes Care.* 2013;36(1):56-62.
62. McDonald SD, Han Z, Mulla S, Beyene J. Overweight and obesity in mothers and risk of preterm birth and low birth weight infants: systematic review and meta-analyses. *BMJ.* 2010;341:c3428.
63. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA.* 2009;301(6):636-50.
64. Calabrese S, Mandò C, Mazzocco MI, Anelli GM, Novielli C, Cetin I. Placental Biometry in Male and Female Fetuses of Obese and Normal Weight Women. *Reprod Sciences.* 2014;21(3 Suppl):151A.
65. Barker, D. J., P. D. Gluckman, K. M. Godfrey, J. E. Harding, J. A. Owens and J. S. Robinson. Fetal nutrition and cardiovascular disease in adult life. *Lancet.* 1993;341(8850):938-41.
66. Zhu MJ, Du M, Nathanielsz PW, Ford SP. Maternal obesity up-regulates inflammatory signaling pathways and enhances cytokine expression in the mid-gestation sheep placenta. *Placenta.* 2010;31(5):387-91.

67. Cetin I, Parisi F, Berti C, Mandò C, Desoye G. Placental fatty acid transport in maternal obesity. *J Dev Orig Health Dis.* 2012;3(6):409-14.
68. Wu G, Imhoff-Kunsch B, Girard AW. Biological mechanisms for nutritional regulation of maternal health and fetal development. *Paediatr Perinat Epidemiol.* 2012;(Suppl 1):4-26.
69. Kapadia MZ, Park CK, Beyene J, Giglia L, Maxwell C, McDonald SD. Weight Loss Instead of Weight Gain within the Guidelines in Obese Women during Pregnancy: A Systematic Review and Meta-Analyses of Maternal and Infant Outcomes. *PLoS One.* 2015;10(7):e0132650.
70. Dabelea D, Mayer-Davis EJ, Lamichhane AP, D'Agostino RB Jr, Liese AD, Vehik KS, Narayan KM, Zeitler P, Hamman RF. Association of intrauterine exposure to maternal diabetes and obesity with type 2 diabetes in youth: the SEARCH Case-Control Study. *Diabetes Care.* 2008;31(7):1422-6.
71. Reynolds RM, Allan KM, Raja EA, Bhattacharya S, McNeill G, Hannaford PC, Sarwar N, Lee AJ, Bhattacharya S, Norman JE. Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring: follow-up of 1 323 275 person years. *BMJ.* 2013;347:f4539.
72. Whitaker RC. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. *Pediatrics.* 2004;114:e29-36.
73. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med.* 1997;337:869-73.
74. Sewell MF, Huston-Presley L, Super DM, Catalano P. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. *Am J Obstet Gynecol.* 2006;195:1100-3.
75. Li C, Kaur H, Choi WS, Huang TT, Lee RE, Ahluwalia JS. Additive interactions of maternal prepregnancy BMI and breastfeeding on childhood overweight. *Obes Res.* 2005;13:362-71.
76. Cesare Marincola F, Dessì A, Corbu S, Reali A, Fanos V. Clinical impact of human breast milk metabolomics. *Clin Chim Acta.* 2015 Feb 14. [Epub ahead of print].
77. Martin FP, Moco S, Montoliu I, Collino S, Da Silva L, Rezzi S, Prieto R, Kussmann M, Inostroza J, Steenhout P. Impact of breastfeeding and high- and low-protein formula on the metabolism and growth of infants from overweight and obese mothers. *Pediatr Res.* 2014;75(4):535-43.
78. Alfaradhi MZ, Ozanne SE. Developmental programming in response to maternal overnutrition. *Front Gene.* 2011;2:27.
79. Berti C, Biessalski HK, Gärtner R, Lapillonne A, Pietrzik K, Poston L, Redman C, Koletzko B, Cetin I. Micronutrients in pregnancy: current knowledge and unresolved questions. *Clin Nutr.* 2011;30(6):689-701.
80. Buckley AJ, Jaquiere AL, Harding JE. Nutritional programming of adult disease. *Cell Tissue Res.* 2005;322(1):73-9.
81. Moran LJ, Sui Z, Cramp CS, Dodd JM. A decrease in diet quality occurs during pregnancy in overweight and obese women which is maintained post-partum. *Int J Obes (Lond).* 2013;37(5):704-11.
82. Josefson JL, Feinglass J, Rademaker AW, Metzger BE, Zeiss DM, Price HE, Langman CB. Maternal obesity and vitamin D sufficiency are associated with cord blood vitamin D insufficiency. *J Clin Endocrinol Metab.* 2013;98(1):114-9.
83. Kim H, Hwang JY, Kim KN, Ha EH, Park H, Ha M, Lee KY, Hong YC, Tamura T, Chang N. Relationship between body-mass index and serum folate concentrations in pregnant women. *Eur J Clin Nutr.* 2012;66(1):136-8.
84. Salam RA, Das JK, Bhutta ZA. Multiple micronutrient supplementation during pregnancy and lactation in low-to-middle-income developing country settings: impact on pregnancy outcomes. *Ann Nutr Metab.* 2014;65:4-12.
85. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2012;11:CD004905.
86. WHO. Iodine deficiency in Europe: a continuing public health problem. Geneva: WHO, 2009.
87. Berti C, Fekete K, Dullemeijer C, Trovato M, Souverein OW, Cavelaars A, Dhonukshe-Rutten R, Massari M, Decsi T, Van't Veer P, Cetin I. Folate intake and markers of folate status in women of reproductive age, pregnant and lactating women: a meta-analysis. *J Nutr Metab.* 2012;2012:470656.
88. Vucic V, Berti C, Vollhardt C, Fekete K, Cetin I, Koletzko B, Gurinovic M, van't Veer P. Effect of iron intervention on growth during gestation, infancy, childhood, and adolescence: a systematic review with meta-analysis. *Nutr Rev.* 2013;71(6):386-401.
89. Catov JM, Bodnar LM, Olsen J, Olsen S, Nohr EA. Periconceptional multivitamin use and risk of preterm or small-for-gestational-age births in the Danish National Birth Cohort. *Am J Clin Nutr.* 2011;94(3):906-12.
90. Moos MK, Dunlop AL, Jack BW, Nelson L, Coonrod DV, Long R, Boggess K, Gardiner PM. Healthier women, healthier reproductive outcomes: recommendations for the routine care of all women of reproductive age. *Am J Obstet Gynecol.* 2008;199:S280.
91. Brantsaeter AL, Myhre R, Haugen M, Myking S, Sengpiel V, Magnus P, Jacobsson B, Meltzer HM. Intake of probiotic food and risk of preeclampsia in primiparous women: the Norwegian Mother and Child Cohort Study. *Am J Epidemiol.* 2011;174(7):807-15.
92. Brantsaeter AL, Birgisdottir BE, Meltzer HM, Kvaalem HE, Alexander J, Magnus P, Haugen M. Maternal seafood consumption and infant birth weight, length and head circumference in the Norwegian Mother and Child Cohort Study. *Br J Nutr.* 2012;107(3):436-44.
93. Papadopoulou E, Caspersen IH, Kvaalem HE, Knutsen HK, Duarte-Salles T, Alexander J, Meltzer HM, Kogevinas M, Brantsaeter AL, Haugen M. Maternal dietary intake of dioxins and polychlorinated biphenyls and birth size in the Norwegian Mother and Child Cohort Study (MoBa). *Environ Int.* 2013;60:209-16.
94. Vejrup K, Brantsaeter AL, Knutsen HK, Magnus P, Alexander J, Kvaalem HE, Meltzer HM, Haugen M. Prenatal mercury exposure and infant birth weight in the Norwegian Mother and Child Cohort Study. *Public Health Nutr.* 2014;17(9):2071-80.