REVIEW ARTICLE

Supplementation during pregnancy: beliefs and science

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Abstract

Pregnancy represents a challenge from a nutritional perspective, because micronutrient intake during the periconceptional period and in pregnancy affects fetal organ development and the mother's health. Inappropriate diet/nutrition in pregnancy can lead to numerous deficiencies including iron deficiency and may impair placental function and play a role in miscarriage, intrauterine growth restriction, preterm delivery, and preeclampsia. This article reviews the risks associated with nutrient deficiencies in pregnant women and presents an overview of recommendations for dietary supplementation in pregnancy, focusing on oral iron supple-mentation. Risk factor detection, including dietary patterns and comorbidities, is paramount in optimal pregnancy management. Dietary habits, which can lead to deficiencies (e.g., iron, folate, vitamin D, and calcium) and result in negative health consequences for the mother and fetus/newborn, need to be investigated. Prenatal care should be personalized, accounting for ethnicity, culture, education, information level about pregnancy, and dietary and physical habits. Clinicians should make a plan for appropriate supplementation and prophylaxis/ treatment of nutritional and other needs, and consider adequate intake of calcium, iodine, vitamin D, folate, and iron. Among the available oral iron supplements, prolonged-released ferrous sulfate (ferrous sulfate–polymeric complex) presents the lowest incidence of overall and gastrointestinal adverse events, with positive implications for compliance.

Introduction

Numerous pregnancy-related myths and mixed messages exist, particularly relating to diet and supplementation, with variations due to cultural differences (in and between countries) and, within societies, due to socioeconomic and educational aspects (Box 1) [1–3]. Although the majority of women turn to medical sources to find out what to expect during pregnancy, even educated women can be influenced by myths. Research conducted among pregnant women in the New York metropolitan area showed that women are strongly influenced about their pregnancies by common hearsay in their social circles and in entertainment media, a phenomenon that is referred to as ''pregnancy mythologies'' fragmentary, contradictory, and elusive forms of knowledge [4].

Historical myths relating to the intake of individual dietary components also exist. For example, in the 1990s, the Danish National Board of Health advocated that iron intake during pregnancy should be increased by a change in diet, recommending a higher intake of, for example, liver paste, spinach, and parsley. However, pregnant women do not appear to change their dietary habits [5], and subsequent studies have highlighted the need for oral iron supplements during pregnancy.

This review article is based on the symposium ''Pregnancy Management: Beliefs and Science'', held at the Annual Meeting of the European Society for Human Reproduction and Embryology (ESHRE) 14 17 June 2015 in Lisbon, Portugal. It is the second in a series on ''Gynecological Care'' [6] and discusses the need for

gynecologists/obstetricians who are caring for pregnant women to investigate their clients' dietary habits, to consider that supplementation is a medical issue, and to focus on clinical evidence relating to the tolerability of oral iron supplementation.

Dietary habits: investigate!

While many myths about dietary habits during pregnancy are cultural/traditional (Box 1), some (e.g., that a pregnant woman should ''eat for two'') may actually endanger pregnant women. Between 2000 and 2002, almost 30% of all direct and indirect pregnancy-related deaths in the UK occurred in women with a body mass index (BMI) 30 [7]. Many common complications and adverse outcomes, at all stages of pregnancy and in the puerperium, are associated with maternal obesity. These include maternal morbidity (miscarriage, pulmonary embolism, venous thromboembolism, gestational diabetes mellitus, dysfunctional labor, postpartum hemorrhage, wound infections, iron deficiency [ID], and anemia) as well as fetal morbidity (congenital anomalies, placental problems, prematurity, large-for-gestational-age babies, and stillbirth), and postpartum problems (neonatal health, lower breast-feeding rates, and obesity among offspring) [8–10]. These perinatal risks can be minimized by identifying at-risk women and implementing a special and individual antenatal care plan [11]. Nevertheless, despite the availability of specific weight gain recommendations in pregnancy [12], between 30 and 60% of pregnant women do not receive weight gain advice [13].

Vegetarianism is an increasingly common dietary choice for many women of childbearing age. Although the implications of vegetarian diets in pregnancy and potential impact on maternal/ fetal outcomes remain unclear, it is important for gynecologists/ obstetricians to investigate this aspect in pregnancy. A recent systematic review evaluated 22 studies of vegetarian/vegan diets in pregnancy [14]. Although none of the studies reported an increase in severe adverse outcomes, nine heterogeneous studies on microelements and vitamins suggested that vegan–vegetarian women may be at risk of vitamin B_{12} and iron deficiencies.

Iron, folate, vitamin D and, to a lesser extent, calcium and iodine, are the most common dietary deficiencies which are of greatest clinical importance in pregnant women.

Vitamin D

A review of published studies linking maternal vitamin D status during pregnancy with maternal, fetal, and postnatal outcomes reported that 26–98% of pregnant women from the US, Australia, the Middle East, and South Asia at or near term were vitamin D-deficient, whereas 66–100% were insufficient [15]. Vitamin D deficiency in the 1st trimester does not seem to be associated with adverse pregnancy outcomes, although the high percentage, i.e., 70%, of insufficient/deficient women highlights the prevalence of vitamin D deficiency in young women of reproductive age [16]. A study conducted in the Netherlands demonstrated a particularly high prevalence of vitamin D deficiency in pregnant non-Western women compared with Western women [17]. In a longitudinal study of healthy pregnant ethnic Danish women from 18 weeks gestation to 8 weeks postpartum, 1.4 3.4% displayed vitamin deficiency and 16 19% vitamin D insufficiency. There was a significant decrease in vitamin D levels from 32 to 39 weeks gestation and from delivery to 8 weeks postpartum. Median dietary vitamin D intake in women of reproductive age was low, 2.4 mg/d [18]. Data from Poland indicate a high degree of vitamin D deficiency in neonates independent of which season of the year they were born [19].

In an evaluation of more than 2100 mothers from the Collaborative Perinatal Project, an observational cohort con-ducted in 12 medical centers in the USA from 1959 to 1965, maternal 25-hydroxyvitamin D levels 37.5 nmol/L versus 537.5 nmol/L in the 1st trimester were associated with half the risk of small for gestational age (SGA; adjusted odds ratio 0.5; 95% CI 0.3 0.9), but no 2nd trimester association was observed [20].

Folate

Based on the median folate levels reported in a systematic review of 62 studies in pregnant women from developed countries, folate intakes in all regions were between 13% and 63% below recommendations in pregnancy (Figure 1) [21]. In a longitudinal study of healthy ethnic Danish pregnant women, plasma and red cell folate demonstrated a gradual, significant decrease from 18 weeks gestation to 8 weeks postpartum and concurrently plasma homocysteine displayed a gradual, significant increase. The prevalence of very low plasma

and red cell folate levels increased from 0.6% during pregnancy to 18% 8 weeks postpartum. Although non-pregnant Danish women of reproductive age have a sufficient dietary folate intake, the increased demands during pregnancy imply a low folate status in late pregnancy and postpartum [22]. In addition to the well-documented association between folate supplementation and prevention of neural tube defects (NTDs) [23,24], periconceptional folic acid use is associated with epigenetic changes in insulin-like growth factor 2 in the child that may affect intrauterine programing of growth and development with consequences for health and disease throughout life [25]. Supplemental folate was also associated with higher live birth rates after assisted reproductive technology treatment [26], and reduced risks of spontaneous abortion [27], and congenital heart defects [28].

Iron

Average iron intakes are also below nutrient recommendations in all developed countries [21]. ID is the most common nutritional deficiency disorder in the world, particularly in developing countries. In the USA, it is estimated that 18% of pregnant women (28.4% in the 3rd trimester) have ID [29]. In Germany, more than 40% of pregnant women (up to 28 weeks of gestation) have ID [30]. Among healthy ethnic Danish pregnant women not taking oral iron supplements, 50% developed ID and 21% iron-deficiency anemia (IDA) whereas among women taking 66 mg ferrous iron daily, only 10% displayed ID and none IDA [31].

Maternal anemia is associated with a number of adverse pregnancy outcomes for the mother (e.g., preeclampsia and increased mortality), fetus (e.g., low birth weight, prematurity, and reduced iron stores), and offspring (e.g., metabolic syndrome and schizophrenia) [32–34]. A prospective cohort study of 1274 pregnant women aged 18 45 years in the UK showed that there was a positive relationship between total iron intake (from food and supplements) in early pregnancy and birth weight [32]. There was also a positive relationship between taking iron-containing supplements in the 1st trimester and hemoglobin (Hb) at 12 and 28 weeks, and mean corpuscular volume (MCV) at 28 weeks [32]. A recent analysis of data from the Baby's Vascular Health and Iron in Pregnancy (Baby VIP) study in the UK, showed that maternal serum ferritin levels515 mg/L at 12 weeks gestation was the strongest predictor (two-fold increased risk) of SGA. The study also showed that for every 10 g/L increase in maternal Hb level in the first half of pregnancy, the risk of SGA was reduced by 30%; levels5110 g/L were associated with a three-fold increase in the risk of SGA [35].

A range of dietary factors can influence iron absorption [36]. Phenolic compounds (e.g., tea, coffee, cocoa, and red wine) have an in vitro inhibitory effect on iron absorption. Phytates present in cereals, seeds, nuts, vegetables, and fruit strongly inhibit iron absorption in a dose-dependent manner; calcium also markedly interferes with the absorption of iron. In contrast, ascorbic acid, in both natural and synthetic forms, is the most potent enhancer of iron absorption. Therefore, ascorbic acid intake at meals should be increased [36]. Vitamin A can prevent the inhibitory effect of simultaneously consumed coffee, tea, and phytates on iron absorption. Meat, fish, and poultry promote non-heme iron absorption by the so-called ''meat factors''. Heme-iron absorption is dependent on body iron status and is inhibited by calcium, not by other dietary factors. Based on this knowledge, it is recommended that heme-iron intake should be increased.

It has previously been established that iron status in women of reproductive age is closely associated with the duration and intensity of menstrual bleeding, which in turn is influenced by both genetic factors and methods of contraception. The longer the bleeding period, the lower the iron status. Consequently, contraceptive pill users have a higher iron status than non-users due to lower menstrual blood losses [37]. A recent study evaluated anamnestic risk factors for ID in pregnancy [30]. Using a combination of a dietary protocol and questionnaire, the risk of ID in gestations of 21 weeks or more could be estimated. The probability of ID and/or anemia increased if menstrual bleedings lasted 6 d, and the tampons used had a high absorbency. The authors concluded that pregnant women should be screened using a questionnaire recording dietary and non-dietary risk factors for ID and that, in addition to determining Hb levels, iron status markers (serum ferritin, soluble transferrin receptor, and transferrin saturation) should be assessed in high-risk women. This allows the recommendation of targeted physician-based iron supplements [30].

Supplementation: a medical issue

From a nutritional perspective, pregnancy is a challenge because the maternal body has to cope with the demanding nutritional supplies of the placenta and the fetus. Nutrients required by the fetus undergo separate metabolism in the maternal body, the placenta and the fetus [38]. Micronutrient intake in the periconceptional period and pregnancy affects embryo/fetal organ development, and may, therefore, have potential effects concerning teratogenicity. Nutrition in pregnancy may influence placental function and may have an impact on fertility, and the frequency of miscarriage, intrauterine growth restriction, preterm delivery, and preeclampsia. In the post-partum period, ID may impact maternal health and impair neonatal nutrition. Consequently, deficiencies during pregnancy and/or lactation may have long-lasting effects on both maternal (e.g., osteoporosis) and infant health as well as on adult-programmed health [38].
Pregnancy requires only a modest increase in energy intake compared with pre-pregnancy requirements (approximately 100 and 300 kcal/d more in the 1st and 2nd/3rd trimesters, respectively), with increased requirements during breastfeeding of 450 kcal/d. However, a very important issue is that the recommended intake for several nutrients shows a much greater increase than the recommended energy intake (Figure 2) [39].
In addition to the complexities of pregnancy itself, geographic/ sociodemographic differences need to be considered regarding nutrient deficiencies in pregnancy. The World Health Organization (WHO) recognizes that vitamin A, iodine, vitamin D, and calcium deficiencies in pregnant women are more common in low than in high income countries, whereas iron and folate deficiency in pregnancy is common worldwide. However, from a practical point of view, only folate and iron supplementations are strongly recommended. An overview of WHO recommendations for nutritional supplementations in pregnant women is shown in Box 2.

Vitamin A supplementation

European Food Safety Authority recommended dietary allowances for vitamin A intake in pregnancy and lactation are 700 mg retinol equivalent (RE)/d and 1300 mg RE/d, respectively [40]. The WHO does not recommend vitamin A supplementation during pregnancy as part of routine antenatal care for the prevention of maternal and infant morbidity and mortality [41]. However, in areas with a severe public health problem related to vitamin A deficiency, vitamin A supplementation during pregnancy is strongly recommended for the prevention of night blindness [41].

Iodine supplementation

Maternal iodine deficiency during pregnancy may have adverse effects on the cognitive function of offspring [42]. Although the recommended median urinary iodine concentration in pregnant women is 150 mg/L, large variations have been reported across different countries worldwide [42 48], with many studies reporting median values5150 mg/L. Dietary sources of iodine include iodized table salt, milk, and mineral water; while WHO/UNICEF guidance recognizes the importance of access to iodized table salt, one of the best and least expensive methods of preventing iodine deficiency [49], recommendations in pregnancy are generally lacking and further research is required to define optimal iodine intake and the potential impact on clinical outcomes.

Vitamin D supplementation

Vitamin D supports maternal and fetal bone health, and high vitamin D status during pregnancy may enhance bone mineralization in offspring [50]. Vitamin D also enables maternal immunological adaptation required to maintain a normal pregnancy, and vitamin D supplementation benefits immune function and the loss of tolerance of preeclampsia [51]. Indeed, increased vitamin D levels are associated with long-term protection against immunological diseases (e.g., allergies, type 1 diabetes, and asthma) [50]. However, although a large proportion of pregnant women are vitamin D-depleted, available evidence directly assessing the benefits and possible disadvantages of vitamin D supplementation is limited. Consequently, vitamin D supplementation is not recommended during pregnancy to prevent the development of preeclampsia and its complications, or as

part of routine antenatal care [52]. There is a strong need for future well-designed intervention studies. Pregnant women should be encouraged to receive adequate nutrition, which is best achieved through the consumption of a healthy balanced diet [52].

Calcium supplementation

In populations where calcium intake is low, WHO recommends that all pregnant women, particularly those at high risk of gestational hypertension, receive 1.5 2.0 g elemental calcium/ day, divided into three doses and preferably taken with meals, from 20 weeks' gestation until the end of pregnancy [53].

Iron supplementation

Compared with pre-pregnancy levels, iron requirements double during pregnancy (Figure 2), resulting from fetal and placental development, and also because of red blood cell expansion [54].
Inadequate iron stores result in IDA (defined as Hb levels 5110 g/L [1st and 3rd trimesters] or5105 g/L [2nd trimester]) [55,56]. Approximately 45 million pregnant women worldwide (&2.5 million women in Europe) have IDA [57]. Moreover, women do not make substantial changes in their dietary habits when they become pregnant, and a higher dietary intake with a higher iron bioavailability would imply fundamental changes in nutritional patterns which are unrealistic in pregnant women [5]. Consequently, iron supplementation is indicated unless iron stores of about 500 mg are present at the beginning of pregnancy (achieved by approximately 15–20% of women in Western countries). In Europe, the majority of women of reproductive age have a low iron status with a median plasma ferritin of &40 mg/ L, corresponding to mobilizable body iron reserves of 200–300 mg [58]. In Western countries, preconceptional or early 1st trimester plasma ferritin should indicate the need for supplementation (general prevention of IDA, or IDA treatment with a specific regimen). Recommendations for individual iron prophylaxis for IDA in pregnancy, according to preconceptional/1st trimester iron status, are shown in Table 1 [33,59–63]. For the general prevention of anemia, the International Nutritional Anemia Consultative Group recommends that in areas with a540% prevalence of anemia in pregnancy (i.e., most industrialized countries), oral ferrous iron 60 mg/d should be administered during pregnancy. In regions with a higher prevalence of anemia, the same daily supplementation (iron 60 mg) should be given throughout pregnancy and continued for 3 months postpartum [64]. Depending on anemia severity, international guidelines recommend elemental ferrous iron 120 mg daily [56,65,66], 100 200 mg daily [67,68], or 60 mg twice daily [69] as first-line IDA treatment. Indeed, the myth of a high-iron diet to prevent or treat IDA is false, with the high physiological requirement for iron during pregnancy being difficult to meet with most diets. Therefore, pregnant women should routinely receive iron supplements, preferably tailored according to their iron status (serum ferritin).
Importantly, the use of daily multivitamin-multimineral supplements, designed specifically for pregnant women is not generally advocated for iron prophylaxis because the amount of iron in such products is often less than 30 mg; furthermore, the absorption of iron from these supplements has not been investigated adequately but is probably low due to the absorptive interaction of iron with other divalent metal ions contained in the tablets [70].

Folic acid supplementation

Folic acid supplementation is recommended for all women of childbearing potential. All women planning pregnancy should take a daily supplement of folic acid 400 mg (additional to the folate content in the diet), starting from 2 months before to 3 months after conception. During the 2nd and 3rd trimesters, continued use of folic acid plus iron supplementation, is recommended for the prevention of anemia, since ID and IDA are often associated with folate deficiency. Evidence also supports the use of folic acid throughout pregnancy for the prevention of preeclampsia. Women at high risk for folate deficiency (e.g., those having a previous child with an

NTD and those taking anticonvulsants associated with development of NTD) should receive supplemental folic acid 4 5 mg/d [71–74].

Which iron supplements should we use in pregnant women?

In general, women have a lower basal metabolism, are more concerned with their body appearance and, consequently, have a lower energy intake and thus iron intake than men [75]. Furthermore, during menstruation, daily iron losses may increase 2–3 times [76] and pregnancy, delivery, and breast-feeding all imply an extra requirement for iron [77].

As noted earlier, ID is the most common nutritional problem worldwide and oral ferrous (bivalent) iron salt formulas are the WHO-recommended drugs of choice for the treatment of ID/IDA [78] because they demonstrate better intestinal iron absorption than ferric (trivalent) iron salt preparations [79], and are more cost effective. Furthermore, the tolerability of oral iron salts is crucial in the treatment of ID, since the high incidence of adverse events (particularly gastrointestinal [GI] events) observed in some studies is associated with low compliance levels [80].

From a practical perspective, oral iron administration is the first choice to replete iron stores as this allows the normal physiological mechanism of GI absorption to be used. Furthermore, oral iron does not imply risk of iron overload and other complications associated with intravenous iron administration. Compared with the oral route, intravenous administration is more costly and complex and is generally reserved for (1) patients with intolerance to oral iron, (2) patients who do not respond to oral iron due to impaired absorption, and (3) patients in whom iron losses are higher than their iron absorption capacity [81]. Iron formulas vary in their composition (different iron salts) and chemical state of iron (ferrous or ferric iron), as well as in their galenic form (immediate-release and prolonged-release formulas) [81]. Ferric iron salt formulas have poor solubility and bioavail-ability (about 3–4 times lower absorption than ferrous sulfate) and need to be transformed into ferrous iron before being absorbed, with potential negative implications for pharmacokinetic inter-individual variability, responder rate and increased number of intakes [81]. Ferrous iron salt preparations usually demonstrate good bioavailability of 10 15%, dependent on body iron status. Consequently, ferrous iron salts are used more widely and are preferred over ferric iron salt preparations [81], with some authors suggesting that ferric supplements should not be used [82,83]. Among oral ferrous preparations, including ferrous sulfate, ferrous fumarate, ferrous gluconate, and prolonged-release ferrous sulfate (ferrous sulfate-polymeric complex FSPC), ferrous sulfate preparations remain an established, standard treatment for ID/IDA given their high effectiveness, acceptable tolerability, and low cost [81].

There are two forms of oral ferrous sulfate preparations, conventional immediate-release products which rapidly release all the iron in the stomach (and are associated with gastric intolerance), and prolonged-release products. A recent study evaluated the serum pharmacokinetics of iron in 30 non-pregnant women with IDA following single oral administration (160 mg) of prolonged-release FSPC (Tardyferon) [84]. Serum iron levels remained elevated up to 12 h after drug intake. The median time to maximum serum iron concentrations occurred 4 h after administration. Between 2 and 8 h post-dosing, mean serum iron concentrations fluctuated by only 20%. The study demonstrated that Tardyferon delivered a prolonged release of iron leading to optimal iron absorption along the main absorptive areas in the small intestines (duodenum-jejunum), thereby decreasing the incidence of GI intolerance [84]. Oral administration of Tardyferon resulted in a significantly higher increase in serum iron levels than immediate-release ferrous sulfate [85]. In a randomized study of 90 pregnant women with IDA at 35 39 weeks of gestation, Tardyferon significantly improved hematologic parameters compared with untreated individuals [86]. Moreover, concurrent with improvements in hematologic parameters, general health and well-being were also superior in Tardyferon recipients, with very good tolerability [86].

A recent systematic review, evaluating the tolerability of oral iron supplements based on data from 111 studies in 10 695 patients, showed that Tardyferon had the lowest incidence of overall (4.1%) and GI (3.7%) adverse events (Figure 3). Of the different oral iron supplements, which have been evaluated, Tardyferon appeared to be the best tolerated ferrous iron preparation [87].

The lower incidence of AEs observed with Tardyferon can be attributed to its galenic formulation, which leads to the extended-release of iron and prevents the build-up of large quantities of elemental iron in the stomach. This effect is compounded by the protective properties of the polymeric complex which is rich in amino sugars that protect the gastrointestinal mucosa. When administered together with ferrous sulfate, most of the iron is liberated once past the gastric tract [88–90].

Conclusions

Dietary habits constitute important risk factors for potentially harmful nutritional deficiencies (e.g., iron, folate, iodine, calcium, and vitamin D) in pregnant women in western countries. Dietary history questionnaires, menstrual pattern questionnaires, and BMI measurement should be considered as an integral part of preconceptional counseling and during the first prenatal visit at the antenatal clinic. Pregnant women at high risk of deficiencies, particularly ID and IDA, require particular attention. Changes in diet may be sufficient to fulfill the requirements of iodine and vitamin D. However, iron and folate supplementation is a medical issue; iron intake should be assessed and its most important biomarker (ferritin) should be measured. Folic acid should be provided before conception and during the 1st trimester to prevent NTD. During the 2nd and the 3rd trimester, folic acid supplementation is needed to compensate for insufficient dietary folate intake. Iron supplementation should be adapted according to the prevention or treatment of ID/IDA. Physicians providing care for pregnant women must bear in mind the need for iron supplements, recognizing that not all iron supplements are the same, particularly regarding the incidence of GI adverse events. Based on a recent systematic review of six oral iron preparations, FSPC Tardyferon displayed the lowest incidence of overall, as well as GI, adverse events.

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Table 1. Individual prophylaxis of iron-deficiency anemia (IDA) with ferrous iron in pregnant women according to iron status (serum ferritin) preconceptional or in the 1st trimester [62].

Serum ferritin (mg/L)	Pregnant women (%)	Management
70–80	15–20	No iron supplement
30–70	40	30–40 mg/d
<30	40	60–80 mg/d

Box 1. Pregnancy-related myths.

Gender

If a wedding ring held over a pregnant woman's abdomen swings in a circle it'll be a girl, if it swings in a line it'll be a boy

If a pregnant woman craves candy, it'll be a girl

Diet and supplementation

A pregnant woman should never eat crab because it is a 'cold natured' food that will cause miscarriage (China)

If you don't eat the food you crave during pregnancy, the baby will have a birthmark in the shape of that kind of food (Japan, Mexico)

Avoid milk because it causes large babies and difficult births (Latin America)

A healthy diet obviates the need for vitamin and mineral supplements

Scientific comment:

Ideally true. Supplements are not a substitute for a healthy diet, but approximately 80% of Americans do not eat the daily foods required for optimal health [1]

Prenatal vitamins cover nutritional needs, fixing poor nutrition

Scientific comment:

Incorrect. The better the nutrition, the greater the benefit of supplements [2]

Supplements must be taken before pregnancy to be beneficial

Scientific comment:

Incorrect. If a woman becomes pregnant prior to taking supplements, she should start taking supplements immediately for greatest benefit during the remainder of pregnancy [3]

Box 2. WHO recommendations for dietary supplementation in pregnant women.

Supplement	Level of evidence/recommendation
Vitamin A	Not recommended in developed countries
Iodine	Need for future research
Vitamin D	Need for future research
Calcium	Recommended in regions with low intake
Folic acid	Strongly recommended
Iron	Strongly recommended

Figure 1. Dietary intake of folate (median and interquartile range) in pregnant women in different regions of the world [21]. The recommended intake of folate in Europe (EU) is 400 mg/d. Adapted from Blumfield et al. A systematic review and meta-analysis of micronutrient intakes during pregnancy in developed countries. Nutr Rev 2013;71:118-32, with permission from Oxford University Press.

Figure 2. Recommended intake of nutrients for pregnant women expressed as a percentage of recommended intake values for non-pregnant women. Data are based on German national consensus recommendations [39]. The recommended intake for several nutrients shows a much greater increase than the recommended energy intake. Adapted from Koletzko et al. German national consensus recommendations on nutrition and lifestyle in pregnancy by the 'Healthy Start-Young Family Network'. Ann Nutr Metab 2013;63:311-22, with permission from Karger Publishers, Basel, Switzerland.

Figure 3. Frequency of (a) overall and (b) gastrointestinal adverse events reported in a systematic review of the tolerability of oral ferrous iron supplements [87]. FSPC, ferrous sulfate–polymeric complex. *p50.001 versus FSPC.

Figure 1.

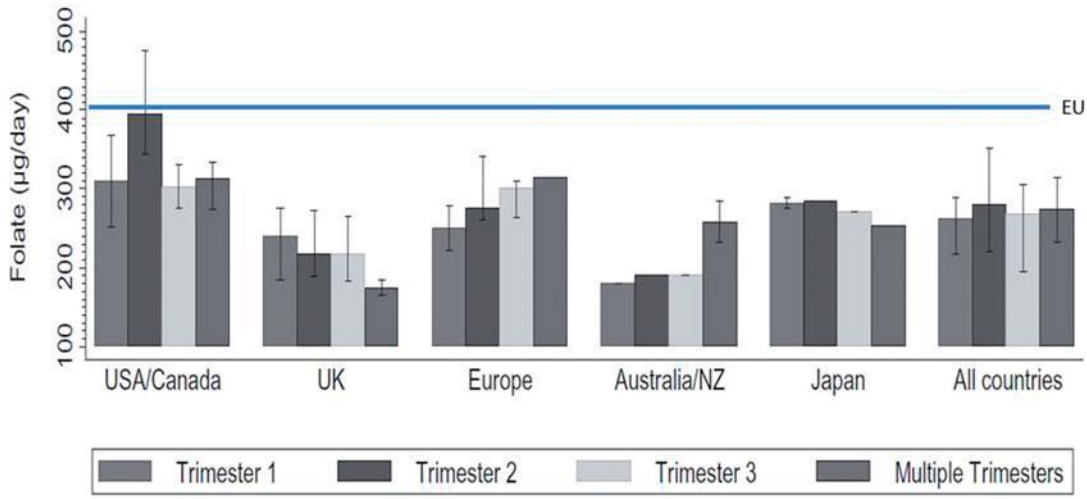

Figure 2.

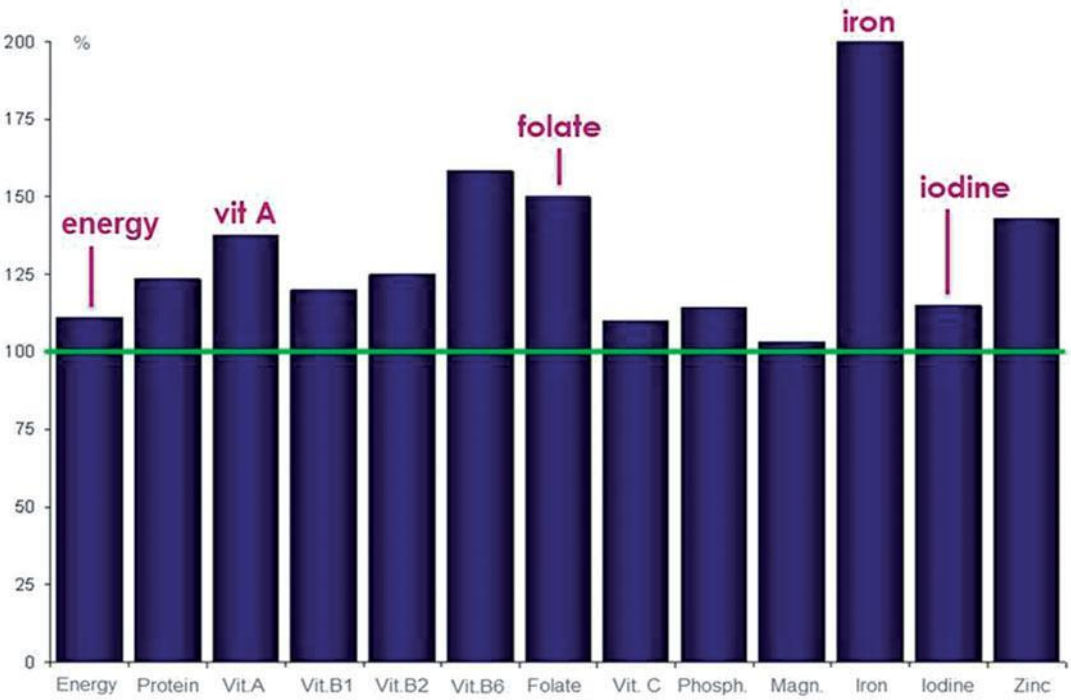

Figure 3a.

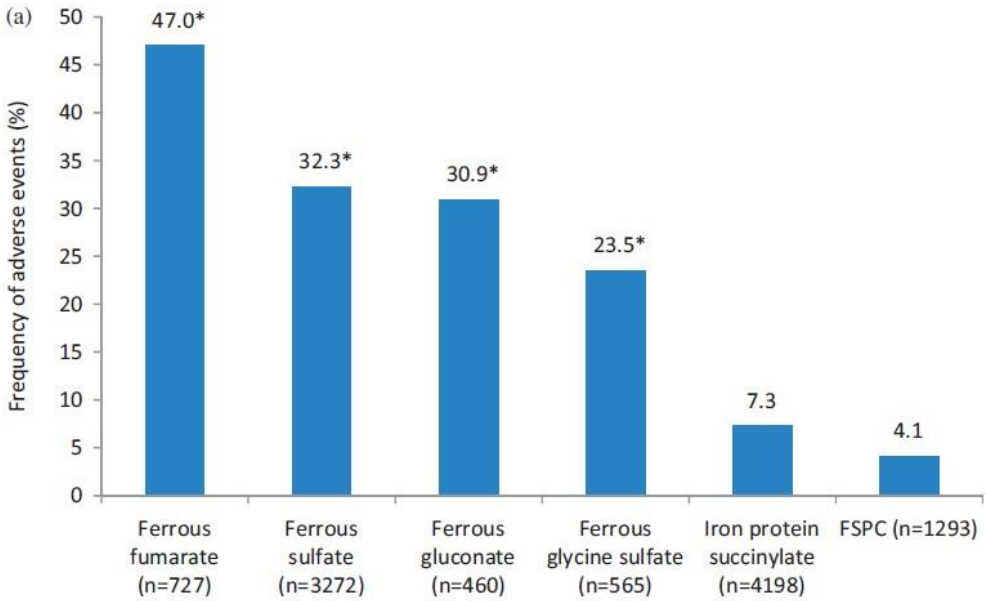

Figure 3b.