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Article in *Annals of Nutrition and Metabolism* · January 2019

DOI: 10.1159/000496471

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Nutrition During Pregnancy, Lactation and Early Childhood and its Implications for Maternal and Long-Term Child Health: The Early Nutrition Project Recommendations

Berthold Koletzko^a K.M. Godfrey^b Lucilla Poston^c
Hania Szajewska^d Johannes B. van Goudoever^e
Marita de Waard^e Brigitte Brands^a Rosalie M. Grivell^f
Andrea R. Deussen^f Jodie M. Dodd^f Bernadeta Patro-Golab^d
Bartłomiej M. Zalewski^d EarlyNutrition Project Systematic Review Group

^aLMU, Ludwig-Maximilians-University of Munich, Dr. von Hauner Children's Hospital, Medical Centre of LMU Munich, München, Germany; ^bMRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK; ^cDivision of Women's Health, Faculty of Life Sciences and Medicine, King's College London, London, UK; ^dMedical University of Warsaw, Department of Paediatrics, Warsaw, Poland; ^eDepartment of Pediatrics, VU University Medical Center, Amsterdam, The Netherlands; ^fDiscipline of Obstetrics and Gynaecology, The Robinson Research Institute, The University of Adelaide, Adelaide, SA, Australia

Keywords

Early nutrition · Lifestyle · Preconception · Pregnancy · Breastfeeding · Infancy · Early childhood · Obesity · Child health · Recommendations · Micronutrients · Metabolic programming · Developmental programming

Abstract

Background: A considerable body of evidence accumulated especially during the last decade, demonstrating that early nutrition and lifestyle have long-term effects on later health and disease ("developmental or metabolic programming").

Methods: Researchers involved in the European Union funded international *EarlyNutrition* research project consolidated the scientific evidence base and existing recommendations

to formulate consensus recommendations on nutrition and lifestyle before and during pregnancy, during infancy and early childhood that take long-term health impact into account. Systematic reviews were performed on published dietary guidelines, standards and recommendations, with special attention to long-term health consequences. In addition, systematic reviews of published systematic reviews on nutritional interventions or exposures in pregnancy and in infants and young children aged up to 3 years that describe effects on subsequent overweight, obesity and body composition were performed. Experts developed consensus recommendations incorporating the wide-ranging expertise from additional 33 stakeholders. **Findings:** Most current recommendations for pregnant women, particularly obese women, and for young children do not take long-term health conse-

quences of early nutrition into account, although the available evidence for relevant consequences of lifestyle, diet and growth patterns in early life on later health and disease risk is strong. **Interpretation:** We present updated recommendations for optimized nutrition before and during pregnancy, during lactation, infancy and toddlerhood, with special reference to later health outcomes. These recommendations are developed for affluent populations, such as women and children in Europe, and should contribute to the primary prevention of obesity and associated non-communicable diseases.

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Introduction

Nutrition and lifestyle before and during pregnancy, lactation, infancy and early childhood have been shown to induce long-term effects on later health of the child, including the risk of common non-communicable diseases such as obesity, diabetes and cardiovascular disease [1–5]. This phenomenon is referred to as “*Early metabolic programming of long-term health and disease*” or “*Developmental origins of adult health and disease*”. The available evidence is based on experimental studies in animals, observations from retrospective and prospective observational studies in human cohorts, increasingly from controlled intervention trials. To strengthen the evidence base, researchers from 36 institutions across the European Union, the United States, and Australia collaborate in the European Commission funded “*EarlyNutrition Research Project*” (<http://www.project-earlynutrition.eu>) [5, 6]. This international multidisciplinary research collaboration explores how nutrition and metabolism during sensitive time periods of early developmental plasticity can have an impact on cytotogenesis, organogenesis, metabolic and endocrine responses as well as epigenetic modification of gene expression, thereby modulating later health. Because of the global escalation in the prevalence of obesity, particular focus has been placed on the developmental origins of adiposity (i.e., body fatness), leading to increasing evidence that early life programming could contribute to the intergenerational transmission of obesity and associated health outcomes [2, 7–9]. The EarlyNutrition Project has received funding from the European Commission (FP7-289346-EARLY NUTRITION), with co-funding provided by the Australian National Health and Medical Research Council (NMHMR), and project partners to achieve a total budget of 11.1 million Euro. The project is

co-ordinated by the Dr. von Hauner Children’s Hospital, LMU – Ludwig-Maximilians-Universität Munich, Germany. The project characterises programming effects and their effect sizes through studying contemporary prospective longitudinal cohort studies, performing randomized controlled intervention trials during pregnancy and infancy, and exploring underlying mechanisms. In order to facilitate translational application, the partnership reviewed available evidence and developed recommendations for dietary practice for women before and during pregnancy and lactation, and for infants and young children, taking long-term health consequences into account. These recommendations are devised for women and children in affluent countries, such as people in Europe.

Methods

The EarlyNutrition Project partners established an international Recommendation Development Panel (RDP) comprised of the project Co-ordinator, Leaders of the Research Project Theme groups, and designated Integrators of the 4 Target Groups to be addressed, that is, women before pregnancy, pregnant and breastfeeding women, infants, and young children. Researchers from the United States and Australia were invited to support this activity. All project partners were invited to propose questions to be explored through systematic reviews of the available evidence. The RDP discussed and prioritised the questions, which was then supported by the assembly of all project partners. Systematic reviews were performed on published dietary guidelines, standards and recommendations during pregnancy (in preparation), in lactation [10] and in children up to the age of 3 years [11], with special attention to recommendations addressing long-term health consequences. In addition, systematic reviews of published data were performed on the impact of paternal and maternal body mass index (BMI) on offspring obesity risk [12], on effects of dietary and lifestyle interventions in pregnant women with a normal BMI [13] and on effects of protein concentration in infant formula on growth and later obesity risk [14]. We also considered the data of systematic reviews on the effects of growth in term infants and later obesity risk [15], the effects of growth in preterm infants on later health [16], on the age of introduction of complementary foods [17], and on the pre- and postnatal effects of dietary iron [18] and of long-chain polyunsaturated fatty acids (LC-PUFA) [19]. Moreover, we performed systematic reviews of published systematic reviews on nutritional interventions or exposures in pregnancy [19] and in infants and young children aged up to 3 years [20] that describe effects on subsequent overweight, obesity and body composition. Based on these results and additional literature contributed by RDP members, recommendations were drafted and discussed and voted upon at a workshop attended by 33 stakeholders with wide-ranging expertise held on May 11, 2016 in Granada, Spain. These experts comprised researchers actively working in the field, representatives of scientific and medical associations (the European Society for Paediatric Gastroenterology, Hepatology

Table 1. Recommendations on preconception nutrition of the FIGO: action points for healthcare providers

Involved professionals	Assessment considerations	Discussion points
– Community health	– Diet composition	– Importance of a healthy diet and exercise
– Workers?	– Physical activity history	– Problems of sedentary behaviour such as screen time
– Nutritionists	– Height, weight, BMI	– Weight loss counselling
– Family doctors/GPs	– Obesity risk	– Risky behaviours and exposures
– Ob-gyns?	– Waist circumference/other anthropometry	– Tobacco, alcohol, recreational drugs
– Midwives	– Anaemia	– Environmental toxins
	– Risk of specific nutritional problems (low nutrient density)	– Chronic disease screening and management
	– Folate	– Supplementation
	– Iron	– Folic acid supplementation 400 µg/day
	– Calcium	– Other as required (iron, iodine, vitamin B12)
	– Vitamin B12	
	– Vitamin D	
	– Iodine	
	– Zinc	
	– Polyunsaturated fatty acids	
FIGO, International Federation of Gynecology and Obstetrics; BMI, body mass index.		

and Nutrition; The International Society for the Developmental Origins of Health and Disease, The US Society of Reproductive Investigation, The Physiological Society, The UK Royal College of Obstetricians and Gynaecologists), and representatives of a parent organisation and the dietetic food industry (European Foundation for the Care of Newborn Infants; Specialised Nutrition Europe). Following intensive discussion, a vote was held on each of the recommendations. According to the guidance from the European Society for Clinical Nutrition and Metabolic Care [21], consensus was defined as >75% of the votes supporting the recommendations, majority agreement as 50–75% of supporting votes, and rejection as <50% of the votes. Voting on the recommendations employed the Delphi method [22]. The recent recommendations of the International Federation of Gynecology and Obstetrics on adolescent, preconception, and maternal nutrition [23] and of the World Health Organisation's Report of the Commission on Ending Childhood Obesity [24] were also reviewed and were generally supported and adopted as the basis of further consideration (29 votes in support, 4 votes abstaining). The draft of this manuscript, which reports the conclusions of the workshop and background information, was shared with all participants and the project partners who were invited to provide further comments and suggestions. RDP members then finalised the manuscript. The revised

and finalized recommendations were then sent out to the experts for final voting. The voting was carried out anonymously using an online voting tool.

Recommendations on Nutrition during Preconception

– Healthcare providers should be encouraged and trained to support and provide advice on preconception nutrition, including optimizing adolescent nutrition and health.

– *Consensus: agreement 34, abstain 0.*

It is widely acknowledged that a focus on preconception health offers an important, newly recognised opportunity for improving the health of future generations [25]. Good health and nutrition before conception are central to a mother's ability to meet the nutrient demands of pregnancy and breastfeeding, and are vital to the healthy

development of her embryo, fetus, infant and child. Many women and adolescent girls are poorly nourished because of the inadequacy or imbalance of their diets, leading to underweight, overweight/obesity and micronutrient deficiencies. Nonetheless, the majority do little to change their lifestyle to prepare for pregnancy [26], even though most pregnancies leading to live births are thought to be – at least to some extent – planned. Consequently, many women have an unhealthy lifestyle as they enter pregnancy, which is characterised by for example, poor quality diet, low levels of physical activity, smoking and excessive alcohol consumption and which remain prevalent around the time of conception. To address this, an International Federation of Gynecology and Obstetrics panel has proposed recommendations for healthcare providers in relation to nutritional status before pregnancy (Table 1) [23], while also encouraging the adoption of good dietary and lifestyle habits at all stages, starting in childhood and adolescence.

Healthy pregnancy outcomes are more likely if women who enter pregnancy are physically active, have a healthy diet, do not smoke, avoid alcohol and have a normal BMI [6, 23]. Addressing preconception nutrition and lifestyle is of particular importance regarding maternal obesity, which has a major influence on both immediate pregnancy outcomes and the child's risk of later becoming obese and contracting non-communicable diseases [23]. Recent intervention studies have shown that in obese pregnant mothers, both pharmacological (metformin) [27, 28] and behavioural (diet/physical activity) interventions [29, 30] during pregnancy have only limited impact on maternal and infant perinatal outcomes, thereby suggesting a need to intervene prior to conception if outcomes are to be improved.

- Healthcare providers should pay particular attention to the body weight and BMI of women of reproductive age, and where appropriate provide advice for modifying body weight by improving diet, lifestyle and physical activity.

- *Consensus: agreement 33, abstain 1.*

Pre-pregnancy BMI is strongly related to health outcomes in mother and offspring, with even stronger effects of pre-pregnancy BMI than of gestational weight gain (GWG) on key outcomes in some studies [31–36]. Due to the increasing prevalence of obesity among women worldwide [37] and recommendations for limiting GWG, several intervention trials have been undertaken in an attempt to find suitable dietary and physical activity regimes that will reduce GWG and improve health outcomes. Most of these intervention studies,

however, have not been of adequate size to provide sufficient statistical power to address pregnancy outcomes. A review of the strategies used has shown a lack of conformity and infrequent attempts to measure the impact of the interventions on diet or physical activity [38]. In a review of 12 randomized controlled trials involving a total of 2,713 pregnant women of normal BMI, Early-Nutrition researchers found that pregnant women of normal BMI who received a dietary and lifestyle intervention were likely to experience less GWG (4 studies, 446 women; mean difference -1.25 kg; 95% CI -2.39 to -0.11), less often reached a GWG exceeding the U.S. Institute of Medicine (IOM) guidelines (4 studies, 446 women; risk ratio 0.66; 95% CI 0.53–0.83) and reduced the incidence of hypertension (2 studies; 243 women; risk ratio 0.34; 95% CI 0.13–0.91). There were, however, no statistically significant differences in the occurrence of gestational diabetes, caesarean section or birth weight greater than 4 kg [13]. Of the few studies that reported childhood follow-up, none reported a lasting benefit on childhood outcomes. A recent Cochrane review of women heterogeneous for BMI reported that interventions based on diet or exercise, or both, reduced the risk of excessive GWG on average by 20%, without major effects on the risks of caesarean delivery, preterm birth, infant macrosomia and poor neonatal outcomes including shoulder dystocia, neonatal hypoglycaemia, hyperbilirubinaemia, or birth trauma [39]. On the basis of current evidence we recommend that there should be a concerted attempt to develop interventions to help women achieve a healthy weight before pregnancy. Undernutrition must not be neglected, as underweight women are more likely to be deficient in important nutrients, and their diets should be carefully assessed and supplemented as required.

- Particular attention should be paid to the intake and status of some micronutrients, especially such as folate, in women of reproductive age. Dietary supplementation with iron, vitamin D, vitamin B₁₂, iodine, and others may be indicated in women at risk of poor supply and insufficiency of these micronutrients.

- *Consensus: agreement 29, abstain 5.*

In pregnancy, the dietary reference intakes for some micronutrients increase much more than the reference intakes for energy; therefore, particular attention should be devoted to an adequate micronutrient supply [40, 41]. Convincing evidence has been established for routine preconception supplementation of folic acid. Plant-based foods including green leafy vegetables, cabbage, legumes, whole grain products, tomatoes and oranges are good di-

etary folate sources, but additional supplementation is strongly advised [42]. Supplementation of at least 400 µg of folic acid per day, commencing prior to conception and continuing into the first trimester of pregnancy, in addition to a folate-rich diet, markedly reduces the risk for serious birth defects, in particular neural tube defects (NTDs) [43–45]. A reduced risk for other congenital birth defects such as congenital heart disease and cleft palate was reported with increased folic acid supply in some but not in all studies [43, 45–50]. While some health professionals give advice on the need for adequate folate status prior to pregnancy for preventing NTDs, many do not [51]. Folate-enriched staple foods should be promoted as an effective strategy to reduce the risk of congenital malformations [45].

Recommendations on Nutrition of Pregnant Women

- Pregnant women should consume a balanced diet in accordance with dietary recommendations for the general population. They should increase dietary energy intake in late pregnancy by no more than about 10% above the recommended energy intake in non-pregnant women.

- *Consensus: agreement 30, abstain 4.*

Much of the recent focus on nutrition in pregnancy relates to the global increase in obesity [37] and the parallel rise in obesity among women in antenatal care. While the consequences for maternal and neonatal outcomes are well recognised, especially gestational diabetes and foetal macrosomia, the potential for longer-term impact on offspring health is not generally appreciated. Early Nutrition researchers, among others, have reported independent associations of maternal obesity, excessive weight gain, as well as diet in pregnancy with childhood adiposity and cardiovascular risk indicators [6, 52–56]. Because of these relationships and the well-established influences of micronutrient deficiencies on foetal development and childhood health, a focus on nutritional status in pregnancy is of paramount importance not only for the health of the mother, but also her offspring.

Unless pre-pregnancy nutrition is sub-optimal, the macronutrient balance in the diet does not need to change in pregnancy. At the beginning of pregnancy, energy requirements differ little from pre-pregnancy. The focus should be on eating a healthy diet with foods rich in critical nutrients, rather than eating more [57]. The concept of “eating for 2” is a myth that should be dispelled. For women with a normal BMI (<25 kg/m²), an increase in energy intake is required only later in pregnancy to pro-

vide for the metabolic demands required of the mother and the energy requirements of the growing foetus. International recommendations suggest that during pregnancy, women increase their energy intake by about 85 kcal per day in the first trimester, 285 kcal per day in the second trimester and 475 kcal per day in the third trimester [23]. However, particularly in the third trimester, the level of physical activity tends to be reduced, such that dietary intake usually does not need to increase by more than about 10% at the end of pregnancy, relative to pre-pregnancy needs [57]. Factors that might indicate a greater energy requirement include adolescent pregnancy (when the mothers own growth places a demand on available nutrients), hard physical labour/high physical activity, multiple pregnancy, and infections or malabsorption disorders, which might decrease nutrient absorption and utilization [23]. Further research is required on energy metabolism and optimal energy intakes in pregnancy in relation to long-term maternal and offspring health outcomes.

- Observational studies support an appropriate increase in weight during pregnancy, but current evidence is insufficient to define optimal GWG for women with different BMI at the beginning of pregnancy. Healthcare providers should focus on advising a healthy diet and lifestyle before and during pregnancy, rather than on prioritizing GWG.

- *Consensus: agreement 27, abstain 7.*

There is lack of consensus for advice on GWG given to pregnant women, which varies extensively between countries [58]. Most widely used are the IOM guidelines (USA) which recommend different ranges of weight gain for normal weight, overweight and obese women [59]. The recommendations originally focussed on the need for adequate maternal GWG to prevent foetal growth restriction, the evidence for which is strong. The recommendations were later extended to include advice for overweight and obese pregnant women. The recommended ranges of weight gain for each BMI category were devised on the basis of available data from observational studies, to prevent small for gestational age and large for gestational age infants, reduce caesarean section rates and prevent post-partum weight retention. Since there is lack of evidence from controlled intervention trials for benefits of applying these recommendations, some expert groups have not recommended adoption of these guidelines for routine clinical practice [57, 58, 60]. In relation to obese pregnant women, gestational diabetes and pre-eclampsia, that is, two of the most common adverse outcomes, were not considered by the IOM due

to the lack of available evidence. Recent studies have also questioned the IOM recommendations for weight gain in obese pregnant women, suggesting that these should be modified according to obesity classes I, II and III (BMI 30–34.9, 35–39.9, and >40 kg/m²) [61]. The most convincing evidence for avoidance of excessive GWG in all BMI categories is the strong association with post-partum weight retention. Even modest post-partum weight retention is associated with heightened risk of adverse outcomes in subsequent pregnancies including hypertensive disease, diabetes and stillbirth [34], and greater attention should be paid to interventions to help women reduce their weight following pregnancy to achieve a healthy BMI.

– We endorse previous recommendations that pregnant women should aim to consume 2 weekly portions of ocean fish, including oily fish. Consumption of large predator fish (e.g., tuna, swordfish) should be limited. Women who do not achieve regular fish consumption should aim to achieve an average total daily intake of at least 300 mg omega-3 docosahexaenoic acid (DHA) by taking a supplement providing at least 200 mg omega-3 DHA per day, in addition to the dietary DHA intake.

– *Consensus: agreement 24, abstain 8.*

Regular consumption of fish as well as supplementation of omega-3 LC-PUFA was found to reduce the risk of early preterm birth prior to 34 weeks of gestation [19]. A recent Cochrane review that included 70 RCTs with 19,927 women at low, mixed or high risk of poor pregnancy outcomes exposed to increased omega-3 LC-PUFA supply for supplements or food compared to placebo or no omega-3. Omega-3 LC-PUFA supply reduced preterm birth <37 weeks (RR 0.89, 95% CI 0.81–0.97) and particularly early preterm birth <34 weeks (RR 0.58, 95% CI 0.44–0.77), while prolonged gestation >42 weeks was increased from 1.6 to 2.6% (RR 1.61, 95% CI 1.11–2.33). There was also no significant trend to reduced infant perinatal death (RR 0.75, 95% CI 0.54–1.03) and fewer neonatal care admissions (RR 0.92, 95% CI 0.83–1.039). Low birthweight was reduced (RR 0.90, 95% CI 0.82–0.99). The mean gestational length was greater in women who received omega-3 LCPUFA (1.67 days, 95% CI 0.95–2.39) and pre-eclampsia may possibly be reduced (RR 0.84, 95% CI 0.69–1.01). The recommended daily intake of n-3 LC-PUFA in pregnancy of 300 mg of DHA [19] can be achieved by eating 2 portions of fish per week, with 1 portion of an oily fish such as mackerel, herring, sardines or salmon [62, 63]. A recent meta-analysis of diet and child growth in 15 European and US cohorts found that a very high fish intake of more than 3

portions per week during pregnancy was associated with higher offspring BMI in early childhood, with a greater effect among girls than boys [64]. A very high consumption of predator fish types like tuna and swordfish, which are at the top of the maritime food chain and may contain high amounts of toxic substances such as methylmercury and lipid soluble pollutants, should be avoided [65] in favour of DHA from other marine sources such as Krill. Pregnant women who do not regularly eat fish or seafood should take a supplement providing at least 200 mg DHA/day, in addition to dietary intake without regular fish consumption that generally provides about 100 mg DHA/day [66].

– Particular attention should be paid to the micronutrient intake in early pregnancy, especially folate. We endorse previous recommendations on folic acid supplementation before conception and in early pregnancy as dietary intake is usually inadequate, and adequate folate status contributes to the prevention of congenital birth defects. Women who may get pregnant are advised to consume 400 µg of folic acid per day as supplements and/or fortified foods.

– *Consensus: agreement 29, abstain 3.*

– Dietary supplementation with iron, vitamin D, vitamin B₁₂, iodine, vitamin A may be indicated in women at risk of poor supply of these micronutrients.

– *Consensus: agreement 29, abstain 4.*

Compared with the modest increase in energy requirements in pregnancy, the requirements of several nutrients, including numerous micronutrients, increase to a much larger extent. Therefore, attention should be directed to dietary quality and the preferential selection of foods rich in critical nutrients, including minerals, vitamins and trace elements. The requirement for many nutrients increase markedly only after the first trimester of pregnancy, whereas an increased intake from conception or even before, relative to non-pregnant women, is recommended for folic acid, iodine and iron.

The need to achieve adequate blood folate concentrations in women of reproductive age to support maternal and offspring health and the prevention of NTDs is widely recognized and based on convincing evidence [43, 45]. Therefore, all women of reproductive age are advised to consume at least 400 µg of folic acid per day as supplements or fortified foods [23]. Folate supplements should be continued during at least the first 16 weeks of pregnancy [45]. As vitamin B₁₂ acts synergistically in the catabolism on homocysteine, which is thought to be related to at least part of the preventive effect, women whose habitual diet is low in vitamin B₁₂

(particularly vegetarian and vegan women) should also consider vitamin B₁₂ supplementation. B vitamins are necessary for optimal health in pregnancy and for foetal growth and brain development. Generally, a balanced diet that includes green vegetables and unprocessed foods should provide adequate folate. Importantly, for lifelong health, folate, vitamin B₁₂ and vitamin B₆, together with choline, are involved in the regulation of DNA methylation status, and deficiencies of these micronutrients may contribute to long-term effects on offspring health through epigenetic pathways [67].

Vitamin D is essential in pregnancy for maintaining maternal calcium homeostasis and thereby for foetal bone development [68–72]. The importance of vitamin D for foetal skeletal development is well recognized; maternal deficiency can result in childhood rickets and osteopenia in the newborn and has also been linked to low birth weight [73, 74], increased risk of neonatal hypocalcaemia, cardiac failure [75] and reduced bone density in childhood [68]. Vitamin D status is contributed by the diet, but the dietary vitamin D intake usually reaches only about 2–4 µg per day [63]. Vitamin D is synthesized in the skin when exposed to sunlight. Spending time outdoors can help to provide a sufficient supply of vitamin D and is encouraged, whereas sunburn should be avoided. Women who live in environments with insufficient sun exposure, who are dark skinned and live in areas of low sun exposure, or whose clothing or use of sunscreen prevents sufficient exposure, are at risk of vitamin D insufficiency. For these women, supplementation should be taken throughout pregnancy. The dose of the vitamin D supplement should be at least 400 IU per day, and the total intake should be in the range of 1,000–2,000 IU per day from dietary sources (e.g., oily fish) and supplements [23, 57]. A recent randomized trial of 1,000 IU of vitamin D supplementation during pregnancy found no effect on offspring bone health in infants born in the summer, but did find enhanced foetal bone mineral accretion in infants born during the winter months [71].

- Pregnant women should avoid taking nutrient supplements at doses markedly exceeding daily reference intakes.

- *Consensus: agreement 30, abstain 3.*

Very high intakes of micronutrients, markedly exceeding requirements, generally do not have benefits but might induce untoward effects and therefore are not recommended. Particular concern exists regarding excessive intakes of vitamin A (retinol) in pregnant women with no evidence of vitamin A insufficiency, which has been as-

sociated with liver dysfunction and birth defects [23]. While a potential risk of larger doses of vitamins C and E on increasing the risk of small for gestational age delivery has been discussed, a systematic review on effects of combined vitamin C and E supplementation during pregnancy suggests no effects on the prevention of foetal or neonatal death, poor foetal growth, preterm birth or pre-eclampsia. It did not detect any effects on the risks of preeclampsia, foetal or neonatal loss, or small for gestational age infants [76].

- Raw animal-based foods, including raw or not thoroughly cooked meat, salami and other raw sausages, raw ham, raw fish, raw seafood, unpasteurized milk, raw eggs, as well as foods made of these products, which are not thoroughly cooked should be avoided during pregnancy.

- *Consensus: agreement 30, abstain 4.*

- Raw fruit and vegetables as well as lettuce should be washed well before consumption, be prepared freshly, and be eaten soon after preparation. Foods grown in or near the ground should be peeled.

- Pregnant women should avoid eating pre-prepared, packaged salads.

- *Consensus: agreement 27, abstain 7.*

- Foods that are grown in or near to the ground should be stored separately from other foods to avoid cross-contamination.

- *Consensus: agreement 26, abstain 7.*

Food-borne illnesses such as listeriosis and toxoplasmosis can cause severe foetal damage, premature birth and stillbirth [77, 78]. Toxoplasmosis may be transmitted via raw or not fully cooked meats and meat products from pork, lamb and game, and with a lesser risk from beef [79–81]. Raw meat products, smoked fish and soft cheeses, unpasteurized milk and products containing unpasteurized milk products, and vegetables and salads may transfer listeriosis [82–86]. *Listeria* can multiply at cool temperatures in a refrigerator, and also in vacuum-sealed packed foods and pre-packed salads. Raw, animal-based foods may also transmit other infections, with particularly high risks in pregnancy, such as salmonellosis.

Recommendations on Nutrition of Breastfeeding Women

- Breastfeeding women should consume a balanced diet providing adequate nutrient intakes and promoting reduction of post-partum weight retention.

- *Consensus: agreement 33, abstain 1.*

– Breastfeeding women should not be encouraged to modify or supplement their diet with the aim to reduce the infant's risk of later overweight or obesity.

– *Consensus: agreement 31, abstain 3.*

Balanced maternal nutrition before and during the breastfeeding period can affect maternal nutrient status and healthy body weight, as well as the infant supply of some nutrients with breastmilk [87]. Effects of the maternal diet during lactation on long-term health in breastfed infants have been reported, but literature on the effects of nutrition of lactating women on their infants' later health is scarce [10, 88, 89]. Most studies focus on the maternal supply of LC-PUFA where there is evidence of a link between fish consumption and higher DHA in breast milk, but no conclusive evidence on effects on infant growth, later body composition or other outcomes [10, 40]. The provision of vitamin D and of live bacteria (so called "probiotics") did not affect the infant's later risk of overweight or obesity [10].

Recommendations on Nutrition in Infants and Young Children

– Feeding practices in infants and young children should aim to achieve a weight gain similar to the normal weight gain defined by generally accepted growth standards.

– *Consensus: agreement 30, abstain 4.*

Rapid weight gain in infancy and in the second year of life, over and above the average weight gain defined by reference growth standards, has been consistently associated with increased subsequent obesity risk in several meta-analyses [2, 15, 90–92]. Weight gain velocity is influenced by feeding practices in infants and young children. Total energy intake, poor diet quality and dietary energy density in early childhood have been associated with later BMI, overweight, and obesity in some studies, although the available evidence is limited [20]. Both under- and overfeeding should be avoided, and energy and nutrient intakes should be adapted to achieve a weight gain similar to the normal weight gain defined by generally accepted growth standards, such as the World Health Organisation growth charts [93].

– Breastfeeding should be promoted, protected and supported. In addition to many other benefits, breastfeeding may contribute to risk reduction for later overweight and obesity.

– *Consensus: agreement 31, abstain 3.*

– Predominant and partial breastfeeding should also be encouraged if exclusive breastfeeding is not achieved.

– *Consensus: agreement 31, abstain 3.*

Breastfeeding is associated with numerous benefits and is universally recommended as the preferred method of infant feeding [94, 95]. Compared with breastfeeding, feeding conventional infant formula induces a higher average weight gain during the first year of life and beyond [96–100]. However, in rare cases, exclusive breastfeeding may also induce excessive weight gain. In some cases, this was observed in association with a higher maternally produced protein content in the breastmilk than normally expected [101–103]. Overall, breastfeeding is associated with a modest risk reduction for later overweight and obesity in childhood and adult life by about 12–14% or more [104–107], although residual confounding cannot be excluded [20]. A very short duration of breastfeeding was associated with a reduced protective effect on the later risk of overweight and obesity as compared to breastfeeding duration of about 6 months or more, although the available evidence is not conclusive and again, residual confounding cannot be excluded [20]. There is no conclusive evidence that exclusive breastfeeding has a stronger protective effect on the later risk of overweight and obesity than predominant or partial breastfeeding, but the data are limited. Partial breastfeeding should also be encouraged if exclusive or full breastfeeding is not achievable.

– Infants born at term who are not breastfed should receive an infant (or from 6 months on a follow-on) formula with a protein supply approaching that provided with breastfeeding.

– *Consensus: agreement 29, abstain 4.*

Lowering the protein content of formula provided to infants, relative to more conventionally used protein contents as advised in the 1980s [108, 109], is a promising intervention that can reduce the risk of later overweight and obesity in children [99, 110]. More studies replicating the reported effects on long-term health outcomes are encouraged [14, 20]. Formula with reduced protein content prevented excessive early weight gain [99, 111–113] and markedly reduced obesity prevalence at early school age [110]. Reducing formula protein also lowered preperitoneal fat content at the age of 5 years, a marker of visceral fat deposition with adverse metabolic consequences [114], and body fat deposition up to early school age [115]. The provision of protein-reduced infant formula in infants of mothers with overweight and obesity, as compared to conventional formula, was reported to provide

considerable long-term health and economic benefits [116].

There is no evidence for beneficial effects on later obesity risk associated with the use of formula for infants based on soy protein isolate or with added non-digestible carbohydrates (so called “prebiotics”), live bacteria (so-called “probiotics”) or LC-PUFAs [20].

– We recommend avoidance of regular cows’ milk or other regular animal milks (other than specially designed and targeted to children using animal milk as a nutrient source) as a drink in the first year of life, and to limit consumption of those dairy milks to about 2 cups per day in the second year of life, whenever feasible and affordable.

– *Consensus: agreement 26, abstain 7.*

Regular cows’ milk and milk of many other animals contain about 3–4 times more protein per unit energy content than human milk or modern infant formula. Feeding infants with regular cows’ milk or other dairy animal milks, such as goat or buffalo milk, particularly as a drink, bears the risk of inducing very high protein intakes. High intakes of protein and particularly of dairy protein during infancy and early childhood, in the order of 10–15% of energy intake or more, have been consistently associated with increased weight gain and a higher risk of later overweight and obesity [20, 100, 117–120]. It appears prudent to avoid cows’ milk as a drink in infancy and to limit cows’ milk to no more than about 2 cups per day in the second year of life whenever feasible and affordable [118, 121, 122].

– Complementary foods should not be introduced before the infant age of 17 weeks and not later than 26 weeks.

– *Consensus: agreement 26, abstain 6.*

– We recommend limiting dietary sugar intake with beverages and foods in infancy and early childhood.

– *Consensus: agreement 30, abstain 3.*

In European and other affluent populations, the introduction of complementary foods is recommended not before 17 weeks and not later than 26 weeks of age for a variety of reasons [95, 121, 123–126]. However, the World Health Organisation recommends exclusive breastfeeding to 6 months and complementary foods to be introduced at the age of 6 months as worldwide guidance, considering the benefits for reducing morbidity and mortality from gastrointestinal and respiratory infectious particularly in low- and low-medium-income countries. Associations between an early introduction of complementary food before 15 weeks of age and later childhood adiposity have been reported in some studies but were not confirmed in others [20].

Variation in the introduction of complementary feeds between 17 and 26 weeks of age was not associated with consistent differences in growth or with alteration of obesity risk [17, 127, 128]. The available systematic reviews do not provide conclusive evidence for associations between certain types or patterns of complementary feeding and subsequent childhood overweight or obesity [20]. Associations between a higher dietary protein intake in early childhood and later childhood overweight or obesity have been reported in some studies [129], whereas there is no conclusive data for a relationship between the intake of fat, dairy products, calcium, fruits and vegetables in early childhood and later BMI or adiposity [20]. Some evidence is suggestive of associations between sugar-sweetened beverage intake in early childhood and the later risk of overweight and obesity [20, 129], but results of different studies are inconsistent and current diet is likely to be a major confounder.

Outlook

The conclusions and recommendations presented here are based on a considered review of currently available data, but in a number of areas, there is still a paucity of available evidence. Progress in scientific understanding over time may enable future updates and revisions of these conclusions. The available evidence for a relevant impact of lifestyle choices, diet and growth patterns in early life on later overweight, obesity, adiposity and associated health outcomes is very encouraging and should prompt markedly enhanced scientific investigation of opportunities for disease prevention and health promotion before and during pregnancy, lactation, and in infancy and early childhood. To facilitate wider dissemination, graphical representation of these recommendations have been developed (cf. online suppl. material, see www.karger.com/doi/10.1159/000496471) and translated into various European languages (<http://www.project-earlynutrition.eu>), and they also serve as the basis for dissemination through a global open-access eLearning platform for healthcare professionals (www.early-nutrition.org).

Acknowledgements

B.K. is supported by the European Commission, H2020 Programmes DYNAHEALTH- 633595 and Lifecycle-733206, the European Research Council Advanced Grant META-GROWTH

ERC-2012-AdG-no.322605, the Erasmus Plus Programmes Early Nutrition eAcademy Southeast Asia-573651-EPP-1-2016-1-DE-EPPKA2-CBHE-JP and Capacity Building to Improve Early Nutrition and Health in South Africa-598488-EPP-1-2018-1-DE-EPPKA2-CBHE-JP, the EU Interreg Programme Focus in CD-CE111 and the European Joint Programming Initiative Project NutriPROGRAM. Further support has been provided by German Ministry of Education and Research, Berlin (Grant Nr. 01 GI 0825), German Research Council (Ko912/12-1 and INST 409/224-1 FUGG), University of Munich Innovation Initiative. K.M.G. is supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre. L.P. is supported by the National Institute for Health Research and the NIHR Biomedical Research Centre at Guy's and St. Thomas' NHS Foundation Trust and King's College London, UK. J.M.D. is supported by an NHMRC Practitioner Fellowship, Australia.

Disclosure Statement

None of the authors declares a conflict of interest with regard to the content of this manuscript, based on the criteria of the US IOM.

Funding Source

Work reported herein is carried out with partial financial support from the Commission of the European Communities, the 7th Framework Programme, contract FP7-289346-EARLY NUTRITION and the European Research Council Advanced Grant ERC-2012-AdG – No. 322605 META-GROWTH. This manuscript does not necessarily reflect the views of the Commission and in no way anticipates the future policy in this area. K.M.G. is supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre. L.P. is supported by the National Institute for Health Research and the NIHR Biomedical Research Centre at Guy's and St. Thomas' NHS Foundation Trust and King's College London, UK. J.M.D. is supported by an NHMRC Practitioner Fellowship, Australia.

Appendix

EarlyNutrition Project Systematic Review Group: *Alberdi G.¹, Buonocore G.², Campoy C.³, Demmelmair H.⁴, Desoye G.⁵, Diaz Gomez M.⁶, Escribano J.⁷, Geraghty A.¹, Gil A.^{8,24}, Hanson M.⁹, Inskip HM.¹⁰, Larque E.¹¹, Lassel T.¹², Luque V.⁷, Mader S.¹³, Manios Y.¹⁴, Mearin L.M.¹⁵, Oddy WH.¹⁶, Reynolds RM.¹⁷, Rueda R.¹⁸, Sherry C.¹⁹, Socha P.²⁰, Taylor P.²¹, Van der Beek E.M.^{12,23}, Weber M.⁴, Crespo-Escobar P.²², Gutser M.⁴, Kouwenhoven S.M.P.²⁵, Calvo-Lerma J.²², Veldhorst M.²⁶

¹UCD Perinatal Research Centre, Obstetrics and Gynaecology, School of Medicine, University College Dublin, National Maternity Hospital, Dublin, Ireland

²Department of Molecular and Developmental Medicine, University of Siena, Italy

³Department of Paediatrics, School of Medicine, University of Granada, Granada, Spain

⁴LMU - Ludwig-Maximilians-University of Munich, Dr. von Hauner Children's Hospital, Medical Centre of LMU Munich, München, Germany

⁵Department of Obstetrics and Gynecology, Medical University of Graz, Graz, Austria

⁶Centro de Investigaciones Biomedicas de Canarias (CIBI-CAN), University of La Laguna, Canary Island, Spain

⁷Paediatrics Research Unit, Universitat Rovira i Virgili, Reus, Spain

⁸Department of Biochemistry and Molecular Biology II, Institute of Nutrition and Food Technology Centre for Biomedical Research, University of Granada, Granada, Spain

⁹Human Development and Health Academic Unit, Faculty of Medicine, NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust (UHSFT) and University of Southampton, Southampton, UK

¹⁰MRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

¹¹Department of Physiology, Faculty of Biology, Campus Mare Nostrum, University of Murcia, Spain

¹²Nutricia Research, Danone Nutricia Early Life Nutrition, Utrecht, The Netherlands.

¹³European Foundation for the Care of Newborn Infants, Munich, Germany

¹⁴Department of Nutrition and Dietetics, Harokopio University of Athens, Athens, Greece

¹⁵Department of Pediatrics, Leiden University Medical Center, Leiden, The Netherlands

¹⁶Menzies Institute for Medical Research, University of Tasmania, Australia

¹⁷Endocrinology Unit, British Heart Foundation Centre for Cardiovascular Science, University of Edinburgh, Queen's Medical Research Institute, Edinburgh, UK

¹⁸Abbott Nutrition Research and Development, Granada, Spain

¹⁹Abbott Nutrition, Scientific and Medical Affairs, Columbus OH, United States

²⁰Children's Memorial Health Institute, Warsaw, Poland

²¹Division of Women's Health, Faculty of Life Sciences and Medicine, King's College London, London, UK

²²Department of Pediatric Gastroenterology, La Fe University Hospital, Valencia, Spain

²³Department of Pediatrics, University Medical Center Groningen, Groningen, The Netherlands

²⁴Iberoamerican Nutrition Foundation, Granada, Spain

²⁵Department of Pediatrics, VU University Medical Center, Amsterdam, the Netherlands

²⁶Department of Epidemiology, Erasmus Medical Centre, Rotterdam, the Netherlands

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