Nutrition in the first 1000 days: emerging research and news

November 2016 - January 2017

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About this report

This report has been commissioned by Nestle Nutrition and produced by the British Nutrition Foundation (BNF). Contents of the report reflect the brief provided by Nestle Nutrition, to give an update on emerging research and news in the area of infant feeding with a particular focus on the first 1000 days (from conception to 2 years). The report is published quarterly and this issue covers the period November 2016 to January 2017. The emerging research section includes the original abstract of each selected paper and BNF comment, where appropriate. Research papers were selected according to the brief and their quality and relevance to future research, policy and guidelines in the area. The news section provides an update on infant feeding policy issues, changes to infant feeding guidelines, new research funding in the area of infant feeding, relevant conferences and other important news. Inclusion of items does not mean endorsement by BNF. The opinion of BNF, where given, is clearly indicated.

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Common abbreviations

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Emerging research

Original research

Background: Iron deficiency (ID) and vitamin D deficiency (VDD) are common among young European children because of low dietary intakes and low compliance to vitamin D supplementation policies. Milk is a common drink for young European children. Studies evaluating the effect of milk fortification on iron and vitamin D status in these children are scarce. Objective: We aimed to investigate the effect of a micronutrient-fortified young-child formula (YCF) on the iron and vitamin D status of young European children. Design: In this randomised, double-blind controlled trial, healthy German, Dutch, and English children aged 1–3 years were allocated to receive either YCF (1.2 mg Fe/100 mL; 1.7 μg vitamin D/100 mL) or non-fortified cow milk (CM) (0.02 mg Fe/100 mL; no vitamin D) for 20 weeks. Blood samples were taken before and after the intervention. The primary and secondary outcomes were change from baseline in serum ferritin (SF) and 25-hydroxyvitamin D [25(OH)D], respectively. ID was defined as SF <12 μg/L in the absence of infection (high-sensitivity C-reactive protein <10 mg/L) and VDD as 25(OH)D <50 nmol/L. Statistical adjustments were made in intention-to-treat analyses for sex, country, age, baseline micronutrient status, and micronutrient intake from food and supplements (and sun exposure in the case of vitamin D outcomes). Results: The study sample consisted of 318 predominantly Caucasian (~95%) children. The difference in the SF and 25(OH)D change between the treatment groups was 6.6 μg/L (95% CI: 1.4, 11.7 μg/L; P = 0.013) and 16.4 nmol/L (95% CI: 9.5, 21.4 nmol/L; P < 0.001), respectively. The probability of ID (OR 0.42; 95% CI:0.18, 0.95; P = 0.036) and VDD (OR 0.22; 95% CI: 0.01, 0.51; P < 0.001) after the intervention was lower in the YCF group than in the CM group. Conclusion: Micronutrient-fortified YCF use for 20 weeks preserves iron status and improves vitamin D status in healthy young children in Western Europe.
BNF COMMENT: This randomised controlled trial (RCT) investigated whether 20 weeks of consumption of micronutrient-fortified young-child formula (YCF) affected the iron and vitamin D status of children aged 1-3 years, when compared to consumption of cows’ milk which has very low levels of both these micronutrients. Results indicate that change from baseline serum concentrations of ferritin and 25-hydroxyvitamin D [25(OH)D] of the children in the micronutrient-fortified YCF group (n=160) increased more than children in the cows' milk group (n=158) (ferritin: 1.7 µL vs -4.9 µL, respectively; 25(OH)D: 9.2 nmol/L vs -7.2 nmol/L, respectively) and the probability of iron deficiency (ID) and vitamin D deficiency (VDD) was significantly decreased following micronutrient-fortified YCF consumption. However, there was no evidence that serum hemoglobin levels and therefore the risk of iron deficiency anemia (IDA) were improved by consumption of micronutrient-fortified YCF. The study used robust RCT methodology that took into account factors that may confound iron and vitamin status variables, such as sun exposure and illness. But as the clinical relevance of increased consumption of iron and vitamin D is largely dependent on low baseline status, consideration must be given to how deficiency was defined in the study. The researchers defined ID as serum ferritin <12µg/L (~19% of the cohort met this criteria) and IDA as serum ferritin <12µg/L combined with a hemoglobin concentration of <110 g/ (~6% of the cohort met this criteria), the latter being used as the primary measure of low iron status by the Department of Health. VDD was defined at serum concentrations <50 nmol/L (37% of the cohort met this criteria), which is higher than the <25 nmol/L threshold used by the Department of Health. Thus, if the UK criteria for low iron and vitamin D status were applied, the benefits of micronutrient-fortified YCF might be less clear. It should also be noted that 95% of the study cohort were White and only 12 of the study participants (3.8%) were from the UK, limiting generalisability of the findings to the UK population. Despite vitamin D being a nutrient of concern in the UK, current advice from the Department of Health is that cows’ milk can be introduced from 1 year and that there is no evidence that fortified formula products for children aged over 1 year provide extra nutritional benefits. To ensure children get enough vitamin D, the Department of Health recommends that children aged 1 to 4 years should be given a daily supplement containing 10 µg of vitamin D. Currently there are no UK recommendations for iron supplementation and most children should be able to get all the iron they need by eating a healthy, varied diet.


Objectives: To determine the associations of breast milk intake after birth with neurological outcomes at term equivalent and 7 years of age in very preterm infants

Study design: We studied 180 infants born at <30 weeks' gestation or <1250 g birth weight enrolled in the Victorian Infant Brain Studies cohort from 2001-2003. We calculated the number of days on which infants received >50% of enteral intake as breast milk from 0-28 days of life. Outcomes included brain volumes measured by magnetic resonance imaging at term equivalent and 7 years of age, and cognitive (IQ, reading, mathematics, attention, working memory, language, visual perception) and motor testing at 7 years of age. We adjusted for age, sex, social risk, and neonatal illness in linear regression. Results: A greater number of days on which infants received >50% breast milk was associated with greater deep nuclear gray matter volume at term equivalent age (0.15 cc/d; 95% CI, 0.05-0.25); and with better performance at age 7 years of age on IQ (0.5 points/d; 95% CI, 0.2-0.8), mathematics (0.5; 95% CI, 0.1-0.9), working memory (0.5; 95% CI, 0.1-0.9), and motor function (0.1; 95% CI, 0.0-0.2) tests. No differences in regional brain volumes at 7 years of age in relation to breast milk intake were observed. Conclusion: Predominant breast milk feeding in the first 28 days of life was associated with a greater deep nuclear gray matter volume at term equivalent age and better IQ, academic achievement, working memory, and motor function at 7 years of age in very preterm infants.

**Background:** Reduced intake of *n*-3 long-chain polyunsaturated fatty acids (LCPUFAs) may be a contributing factor to the increasing prevalence of wheezing disorders. We assessed the effect of supplementation with *n*-3 LCPUFAs in pregnant women on the risk of persistent wheeze and asthma in their offspring.

**Methods:** We randomly assigned 736 pregnant women at 24 weeks of gestation to receive 2.4 g of *n*-3 LCPUFA (fish oil) or placebo (olive oil) per day. Their children formed the *Copenhagen Prospective Studies on Asthma in Childhood 2010* (COPSAC2010) cohort and were followed prospectively with extensive clinical phenotyping. Neither the investigators nor the participants were aware of group assignments during follow-up for the first 3 years of the children’s lives, after which there was a 2-year follow-up period during which only the investigators were unaware of group assignments. The primary end point was persistent wheeze or asthma, and the secondary end points included lower respiratory tract infections, asthma exacerbations, eczema, and allergic sensitization.

**Results:** A total of 695 children were included in the trial, and 95.5% completed the 3-year, double-blind follow-up period. The risk of persistent wheeze or asthma in the treatment group was 16.9%, versus 23.7% in the control group [hazard ratio, 0.69; 95% confidence interval (CI), 0.49 to 0.97; *P*=0.035], corresponding to a relative reduction of 30.7%. Prespecified subgroup analyses suggested that the effect was strongest in the children of women whose blood levels of eicosapentaenoic acid and docosahexaenoic acid were in the lowest third of the trial population at randomisation: 17.5% versus 34.1% (hazard ratio, 0.46; 95% CI, 0.25 to 0.83; *P*=0.011). Analyses of secondary end points showed that supplementation with *n*-3 LCPUFA was associated with a reduced risk of infections of the lower respiratory tract (31.7% vs. 39.1%; hazard ratio, 0.75; 95% CI, 0.58 to 0.98; *P*=0.033), but there was no statistically significant association between supplementation and asthma exacerbations, eczema, or allergic sensitisation.

**Conclusions:** Supplementation with *n*-3 LCPUFA in the third trimester of pregnancy reduced the absolute risk of persistent wheeze, asthma and infections of the lower respiratory tract in offspring by approximately 7 percentage points, or one third.

**BNF COMMENT:** Long chain *n*-3 fatty acids, of which oily fish are a rich source, are an essential fatty acid that must be supplied by the diet and are known to support brain growth and visual development of fetuses *in utero*. This randomised controlled trial (RCT) involving the *Copenhagen Prospective Studies on Asthma in Childhood 2010* (COPSAC2010) cohort provides the first evidence that long chain *n*-3 fatty acid (fish oil) supplementation in the third trimester of pregnancy reduces the risk of persistent wheeze, asthma and infections of the lower respiratory tract in offspring (aged up to 5 years) by about a third. The study used robust RCT methodology and levels of *n*-3 fatty acids in the pregnant women’s blood were assessed using state-of-the-art techniques. However, the dose of long chain *n*-3 fatty acids used in the study was about five times higher than that obtained from consuming one white and one oily portion of fish per week (as recommended by the UK Department of Health). Current advice in the UK for pregnant women is to eat a maximum of two portions of oily fish per week, as it can contain low levels of mercury and pollutants that can build up in the body, and to avoid fish liver oil supplements, because they can contain high levels of vitamin A, both of which can harm a growing fetus. Further work is needed to confirm that intake of long chain *n*-3 fatty acids as fish oil at this level in pregnancy has no detrimental effects on the offspring’s development and to see whether lower doses of long chain *n*-3 fatty acids, and from different sources, can have similar positive effects on the risk of developing persistent wheeze, asthma and infections of the lower respiratory tract in childhood.
Objective: Breastfeeding has been linked to lower rates of childhood obesity. Human milk contains cortisol, known to regulate glucose storage and metabolism. The aim of this study was to test the hypothesis that early exposure to cortisol in human breast milk helps to modulate infant body mass index (BMI) trajectories over the first 2 years of life. Methods: Growth curve modeling was used to examine whether infant exposure to cortisol in human milk at 3 months predicted changes in child body mass index percentile (BMIP) at 6, 12, and 24 months of age in 51 breastfeeding mother–child pairs. Results: Infants exposed to higher milk cortisol levels at 3 months were less likely to exhibit BMIP gains over the first 2 years of life, compared with infants exposed to lower milk cortisol. By age 2 years, infants exposed to higher milk cortisol levels had lower BMIPs than infants exposed to lower milk cortisol. Milk cortisol was a stronger predictor of BMIP change in girls than boys. Conclusions: Cortisol exposure through human milk may help to programme metabolic functioning and childhood obesity risk. Further, because infant formula contains only trace amounts of glucocorticoids, these findings suggest that cortisol in milk is a novel biological pathway through which breastfeeding may protect against later obesity.

Objective: To determine whether a responsive parenting (RP) intervention affects infant dietary patterns. Methods: Primiparous mother-newborn dyads (n=291) were randomised to the Intervention Nurses Start Infants Growing on Healthy Trajectories (INSIGHT) RP intervention or control. Curricula were delivered at nurse home visits at ages 3, 16, 28, and 40 weeks. RP group feeding guidance advised responsive feeding, delayed introduction of solids (to six months), repeated exposure to novel foods, and age-appropriate portion sizes. Latent class analysis identified patterns of dietary exposure at 9 months. Class membership at 9 months was used to predict BMI percentile at 2 years. Results: Five dietary patterns were identified: ‘Breastfed, Fruits and Vegetables’, ‘Breastfed, Low Variety’, ‘Formula, Fruits and Vegetables’, ‘Formula, Low Variety’ and ‘Formula, High Energy Density’. Over 60% of infants had patterns low in fruits and vegetables or high in energy-dense foods. RP group infants were less likely than control to be in the ‘Formula, Low Variety’ class (OR = 0.40, 95% CI 0.23–0.71) or ‘Formula, High Energy Density’ class (OR = 0.28, 95% CI 0.12–0.61) relative to the ‘Formula, Fruits and Vegetables’ class. Dietary pattern at 9 months was significantly associated with BMI percentile at 2 years. Conclusions: While a majority of infants consumed diets low in fruits and vegetables, the INSIGHT RP intervention was associated with healthier dietary patterns.

**Background:** Data from previous studies have suggested a possible association between antibiotic use in infancy and risk of childhood obesity, with implications for health-care delivery and obesity prevention strategies. However, whether the observed association was due to antibiotic use or underlying infection, or both, is unclear. We aimed to disentangle the effect of antibiotic use in infancy from that of underlying infection on the risk of childhood obesity.

**Methods:** In this longitudinal birth cohort study, we included infants in the Kaiser Permanente Northern California population born between 1 January 1997, and 31 March 2013. We used electronic medical records to ascertain data for antibiotic use, infection diagnosis, and anthropometric measurements (and thus BMI and obesity status) from birth up to age 18 years. We used standard mixed-effects logistic regression for repeated measurements to analyse multiple BMI measurements per child (median five measurements) and to obtain odds ratios (ORs) and 95% CIs for obesity risk. We also did a substudy in 547 same-sex twin pairs with discordant exposure status to substantiate our findings.

**Findings:** 260,556 individuals were included in our analysis. After controlling for maternal age, race or ethnic origin, pre-pregnancy BMI, preterm delivery, low birthweight, maternal antibiotic use, and infection during pregnancy, infection without antibiotic use in infancy was associated with an increased risk of childhood obesity compared with controls without infection (OR 1.25, 95% CI 1.20–1.29). A clear dose–response relation was seen between infection...
episodes and risk of childhood obesity ($p$ trend <0·0001). By contrast, compared with infants with untreated infection, antibiotic use during infancy was not associated with risk of childhood obesity (1·01, 0·98–1·04). Neither broad-spectrum nor narrow-spectrum antibiotics were associated with risk of childhood obesity. These findings were supported by the results of the twin set analysis. **Interpretation:** Infection, but not antibiotic use, during infancy is associated with risk of childhood obesity. This finding will need to be replicated in future studies. Although our results do not rule out a potential effect of antibiotics on microbiome composition and the use of antibiotics should always be judicious, they suggest that treatment of common infections with antibiotics in infancy is unlikely to be a main contributor to childhood obesity.


**Importance:** Protein, supplied in currently available commercial fortifiers, may be inadequate to meet the requirements of very preterm infants; in addition, intra-individual and inter-individual variability of human milk protein and energy content potentially contribute to unsatisfactory early postnatal growth. **Objective:** To determine effects on growth of different levels of enteral protein supplementation in predominantly human milk-fed preterm infants. **Design, setting, and participants:** This randomised clinical and partially blinded single-centre trial was conducted in a neonatal tertiary referral centre in Germany. Sixty preterm infants (gestation <32 weeks and weight <1500 g at birth) were recruited from October 2012 to October 2014 and included 35% of 173 eligible infants. Median (interquartile range [IQR]) gestational age at birth was 29.9 (28.7-31.2) weeks. All analyses were conducted in an intention-to-treat population. **Interventions:** Infants were randomly assigned to either a lower-protein (adding 1 g of bovine protein/100 mL of breast milk through a commercial human milk fortifier; $n = 30$) or a higher-protein group at a median (IQR) postnatal age of 7 (6-8) days. The higher-protein group ($n = 30$) received either standardized higher-protein supplementation (study fortifier adding 1.8 g of bovine protein/100 mL of breast milk [$n = 15$]) or individualized high-protein supplementation based on protein and fat content of administered breast milk ($n = 15$). Study interventions were continued for a median (IQR) of 41 (30-57) days and until definite discharge planning. **Main outcomes and measures:** Primary outcome was weight gain (g/kg/d) from birth to the end of intervention. **Results:** Sixty preterm infants (gestation <32 weeks and weight <1500 g at birth), 33 girls, were recruited from October 2012 to October 2014 and included 35% of 173 eligible infants. Median (IQR) gestational age at birth was 29.9 (28.7-31.2) weeks. Demographic characteristics and hospital courses were similar in both groups, and birth weights ranged from 580 to 1495 g in the lower-protein group and 490 to 1470 g in the higher-protein group. Weight gain was similar in the lower- and higher-protein groups: mean (95% CI), 16.3 g/kg/d (15.4-17.1 g/kg/d) in the lower-protein group vs 16.0 g/kg/d (15.1-16.9 g/kg/d) in the higher-protein group ($P = .70$), despite an increase in actual protein intake by 0.6 g/kg/day (0.4-0.7 g/kg/d) ($P < .001$). Head circumference and lower leg longitudinal growth were also similar, as was the proportion of cumulative total enteral feeding volume provided as breast milk: median (IQR) proportion of breast milk, 92% (79%-98%) in the lower-protein group vs 94% (62%-99%) in the higher-protein group ($P = .89$). **Conclusions and
relevance: An increase in protein intake by 0.6 g/kg/day to a mean intake of 4.3 g/kg/day did not further enhance growth of very preterm infants with a median birth weight of 1200 g, who achieved near-fetal growth rates. This might point to a ceiling effect for enteral protein intake with respect to its influence on growth.


Objectives: To evaluate the associations between breastfeeding duration, age at solids introduction, and their interaction in relation to infant (age 9-15 months) above normal body mass index (BMI). Study design: Cross-sectional, population-based study with 3153 infants from Melbourne (2007-2011). Above normal BMI (z score >2, equivalent to >97.7th percentile) defined using the World Health Organization standard. Results: Both longer duration of full and any (full or partial) breastfeeding were associated with lower odds of above normal BMI [e.g. aOR, 0.37 (95% CI, 0.22-0.60) for full breastfeeding 4-5 months versus 0-1 months]. Compared with introduction of solids at 5-6 months, both early and delayed introduction were associated with increased odds of above normal BMI [aOR for 4 months, 1.75 (95% CI, 1.10-2.80) and for ≥7 months, 2.64 (95% CI, 1.26-5.54) versus 6 months]. Such associations differ by breastfeeding status at 4 months (interaction P = .08). Early introduction of solids was associated with increased odds of above normal BMI in both infants fully or partially breastfed for ≥4 months (aOR, 3.66; 95% CI, 1.41-9.51) and those breastfed for <4 months (aOR, 3.11; 95% CI, 1.39-6.97). Introduction of solids at ≥7 months was associated with increased odds of above normal BMI (aOR, 5.79; 95% CI, 1.91-17.49) among infants breastfed for <4 months only. Conclusion: Introduction of solids at 5-6 months, compared with either early or delayed introduction, is associated with decreased odds of above normal BMI at 1 year of age, regardless of infants’ breastfeeding status at 4 months. These results may have implications for public health guidelines with regard to recommendations about the optimal timing of the introduction of solid foods in infancy.
Reviews

Background: In 2010, the diagnosis and treatment of IgE-mediated cow’s milk allergy (CMA) were systematised in a GRADE guideline. Objectives and methods: After 6 years, the state of the knowledge in diagnosis and treatment of CMA has largely evolved. We summarise here the main advances, and exemplify indicating some specific points: studies aimed at better knowledge of the effects of breastfeeding and the production of new special formulae intended for the treatment of CMA. The literature (PubMed/MEDLINE) was searched using the following algorithms: (1) [milk allergy] AND diagnosis; (2) [milk allergy] AND [formul*] OR [breast*], setting the search engine [6-years] time and [human] limits. The authors drew on their collective clinical experience to restrict retrieved studies to those of relevance to a pediatric allergy practice. Results: Several clinical studies did address the possibility to diagnose CMA using new tools in vitro and in vivo, and to diagnose it without any evaluation of sensitisation. Some studies also addressed the clinical role of formulae based on milk hydrolysates, soy, or rice hydrolysates in the treatment of CMA. Many studies have elucidated the effects of selective nutrients in breastfed infants on their immunologic and neurologic characteristics. Conclusions: Evidence-based diagnostic criteria should be identified for non-IgE-mediated CMA. Debate is ongoing about the best substitute for infants with CMA. In particular, Hydrolyzed Rice Formulae have been widely assessed in the last 6 years. In the substitute choice, clinicians should be aware of recent studies that can modify the interpretation of the current recommendations. New systematic reviews and meta-analyses are needed to confirm or modify the current DRACMA recommendations.


Objective: To quantify the association between maternal pre-pregnancy body mass index (BMI) and perinatal outcomes. Methods: We systematically reviewed and collected studies on maternal pre-pregnancy BMI and perinatal outcomes published up to 31 August 2015. For each study, we constructed separate two-by-two tables to calculate the odds ratios (ORs) and 95% confidence intervals (CI). Results: A total of 60 studies involving 1,392,799 women were included, and the proportions of obesity, overweight, normal weight and underweight pregnant women were 11.72%, 22.08%, 58.03% and 8.18%, respectively. When mothers were overweight or obese, their infants had a significantly higher risk of being large for gestational age (OR, 1.45, 95%CI, 1.29–1.63 and 1.88, 95%CI, 1.67–2.11, respectively), having macrosomia (OR, 1.70, 95%CI, 1.55–1.87 and 2.92, 95%CI, 2.67–3.20, respectively), being admitted to the neonatal intensive care unit (OR, 1.29, 95%CI, 1.12–1.48 and 1.91, 95%CI, 1.60–2.29, respectively) and being stillborn (OR, 1.27, 95%CI, 1.18–1.36 and 1.81, 95%CI, 1.69–1.93, respectively). When mothers were underweight, their infants had a lower risk of the aforementioned outcomes. However, mothers who were underweight had a higher risk of preterm birth (OR, 1.30, 95%CI, 1.13–1.49) and delivering an infant small for gestational age (OR, 1.67, 95%CI, 1.49–1.87). Importantly, infants had a higher risk of having a low birth weight (LBW) when their mothers were underweight (OR, 1.67, 95%CI, 1.39–2.02) or obese (OR, 1.24, 95%CI, 1.09–1.41). Conclusion:
Being overweight or obese was associated with an increased risk of still birth, large for gestational age, macrosomia, admission to the neonatal intensive care unit and LBW, while being underweight was associated with an increased risk of preterm birth, small for gestational age, and LBW. Women of childbearing age should maintain a normal body mass index before pregnancy.


Responsive feeding has been identified as important in preventing overconsumption by infants. However, this is predicated on an assumption that parents recognise and respond to infant feeding cues. Despite this, relatively little is understood about how infants engage parental feeding responses. Therefore, the aim of this systematic review was to identify what is known about infant communication of hunger and satiation and what issues impact on the expression and perception of these states. A search of Medline, CINAHL, Web of Science, PsycINFO, Science Direct and Maternal and Infant care produced 27 papers. Eligibility criteria included peer reviewed qualitative and/or quantitative publications on feeding behaviours, hunger, and satiation/satiation cues of typically developing children in the first 2 years of life. Papers published between 1966 and 2013 were included in the review. The review revealed that feeding cues and behaviours are shaped by numerous issues, such as infants’ physical attributes, individual psychological factors and environmental factors. Meanwhile, infant characteristics, external cues and mothers' own characteristics affect how feeding cues are perceived. The existing literature provides insights into many aspects of hunger and satiation in infancy; however, there are significant gaps in our knowledge. There is a lack of validated tools for measuring hunger and satiation, a need to understand how different infant characteristics impact on feeding behaviour and a need to extricate the respective contributions of infant and maternal characteristics to perceptions of hunger and satiation. Further research is also recommended to differentiate between feeding driven by liking and that driven by hunger.

BNF COMMENT: Healthy eating is not only dependent on the types of food and drinks consumed but also on the amount eaten. Hunger, satiation (the within-meal decline in hunger and increase in fullness that leads to the inhibition of further eating) and satiety (the extent to which appetite is suppressed between meals) underpin the ability to self-regulate food intake (i.e. consume appropriate amounts of foods and drinks to meet physiological needs and achieve energy balance). Therefore it’s important that parents are able to identify when their infant is hungry or satiated and respond appropriately to these cues; this forms the basis of responsive feeding. This systematic review aimed to identify research on how appetite cues are expressed in infants, the factors that influence these cues and how parents perceive and respond to these cues. Key findings are that mothers use many cues to assess their infant’s appetite, with hunger cues being the easiest to identify, and that, in general, these cues are easier to interpret as children grow older. Many factors relating to both infant and maternal characteristics play a role in the interactions that occur between mother and infants during feeding and also the influence that infant's appetite cues will have on amount of food consumed. Although a large body of literature was considered in this review, it should be noted that the quality of some of the reviewed papers was considered low, there was significant heterogeneity in methods of investigations, validated tools to assess infant eating behaviours were found to lacking and significant gaps in the literature were identified. Findings from this review will be relevant to people developing interventions and guidance in the area of responsive feeding.

Adequate supply of micronutrients during the first 1000 days is essential for normal development and healthy life. We aimed to investigate if interventions administering dietary doses up to the recommended nutrient intake (RNI) of iron and zinc, within the window from conception to age 2 years, have the potential to influence nutritional status and development of children. To address this objective, a systematic review and meta-analysis of randomised and quasi-randomised fortification, biofortification, and supplementation trials in women (pregnant and lactating) and children (6–23 months) delivering iron or zinc in doses up to the recommended nutrient intake (RNI) levels was conducted. Supplying iron or zinc during pregnancy had no effects on birth outcomes. There were limited or no data on the effects of iron/zinc during pregnancy and lactation on child iron/zinc status, growth, morbidity, and psychomotor and mental development. Delivering up to 15 mg iron/day during infancy increased mean hemoglobin by 4 g/L (p < 0.001) and mean serum ferritin concentration by 17.6 µg/L (p < 0.001) and reduced the risk for anemia by 41% (p < 0.001), iron deficiency by 78% (ID; p < 0.001) and iron deficiency anemia by 80% (IDA; p < 0.001), but had no effect on growth or psychomotor development. Providing up to 10 mg of additional zinc during infancy increased plasma zinc concentration by 2.03 µmol/L (p < 0.001) and reduced the risk of zinc deficiency by 47% (p < 0.001). Further, we observed positive effects on child weight for age z-score (WAZ) (p < 0.05), weight for height z-score (WHZ) (p < 0.05), but not on height for age z-score (HAZ) or the risk for stunting, wasting, and underweight. There are no studies covering the full 1000 days window and the effects of iron and zinc delivered during pregnancy and lactation on child outcomes are ambiguous, but low dose daily iron and zinc use during 6–23 months of age has a positive effect on child iron and zinc status.


Background: Alcohol use during pregnancy is the direct cause of fetal alcohol syndrome (FAS). We aimed to estimate the prevalence of alcohol use during pregnancy and FAS in the general population and, by linking these two indicators, estimate the number of pregnant women that consumed alcohol during pregnancy per one case of FAS. Methods: We began by doing two independent comprehensive systematic literature searches using multiple electronic databases for original quantitative studies that reported the prevalence in the general population of the respective country of alcohol use during pregnancy published from 1 January 1984, to 30 June 2014, or the prevalence of FAS published from 1 November 1973, to 30 June 2015, in a peer-reviewed journal or scholarly report. Each study on the prevalence of alcohol use during pregnancy was critically appraised using a checklist for observational studies, and each study on the prevalence of FAS was critically appraised by use of a method specifically designed for systematic reviews addressing questions of prevalence. Studies on the prevalence of alcohol use during pregnancy and/or FAS were omitted if they used a sample population not generalisable to the general population of the respective country, reported a pooled estimate by combining several studies, or were published in iteration. Studies that excluded
abstainers were also omitted for the prevalence of alcohol use during pregnancy. We then did country-specific random-effects meta-analyses to estimate the pooled prevalence of these indicators. For countries with one or no empirical studies, we predicted prevalence of alcohol use during pregnancy using fractional response regression modelling and prevalence of FAS using a quotient of the average number of women who consumed alcohol during pregnancy per one case of FAS. We used Monte Carlo simulations to derive confidence intervals for the country-specific point estimates of the prevalence of FAS. We estimated WHO regional and global averages of the prevalence of alcohol use during pregnancy and FAS, weighted by the number of livebirths per country. The review protocols for the prevalence of alcohol use during pregnancy (CRD42016033835) and FAS (CRD42016033837) are available on PROSPERO. 

Findings: Of 23 470 studies identified for the prevalence of alcohol use, 328 studies were retained for systematic review and meta-analysis; the search strategy for the prevalence of FAS yielded 11 110 studies, of which 62 were used in our analysis. The global prevalence of alcohol use during pregnancy was estimated to be 9.8% (95% CI 8.9–11.1) and the estimated prevalence of FAS in the general population was 14.6 per 10 000 people (95% CI 9.4–23.3). We also estimated that one in every 67 women who consumed alcohol during pregnancy would deliver a child with FAS, which translates to about 119 000 children born with FAS in the world every year. Interpretation: Alcohol use during pregnancy is common in many countries and as such, FAS is a relatively prevalent alcohol-related birth defect. More effective prevention strategies targeting alcohol use during pregnancy and surveillance of FAS are urgently needed.


What is the issue? Can dietary advice for pregnant women prevent the development of diabetes in pregnancy, known as gestational diabetes mellitus (GDM), which can cause health complications for women and their babies? Why is this important? Women with GDM have an increased risk of developing high blood pressure and protein in their urine during pregnancy (pre-eclampsia), and of having a caesarean section birth. Their babies may grow large and, as a result, be injured at birth, or cause injury to their mothers during birth. Additionally, there can be long-term health problems for women and their babies, including an increased risk of cardiovascular disease or type 2 diabetes. The number of women being diagnosed with GDM is increasing around the world, so finding simple and cost-effective ways to prevent women developing GDM is important. Carbohydrates are the main nutrient affecting blood glucose after meals. The glycaemic index (GI) can be used to characterise the capability of carbohydrate-based foods to raise these levels. Some diets, for example, those with low-fibre and high-GI foods, can increase the risk of developing GDM. It has been suggested that dietary advice interventions in pregnancy may help to prevent women developing GDM. What evidence did we find? We searched for studies on 3 January 2016, and included 11 randomised controlled trials involving 2786 pregnant women and their babies. The quality of the evidence was assessed as low or very low and the overall risk of bias of the trials was unclear to moderate. Six trials compared dietary advice with standard care, four compared advice focused on a low-GI diet with advice for a moderate- to high-GI diet, and one compared dietary advice focused on a high-fibre diet with standard advice. There was a possible reduction in the
development of GDM for women who received dietary advice versus standard care across five trials (1279 women, very low-quality evidence), though no clear difference for GDM was seen between women who received low- versus moderate- to high-GI diet advice across four trials (912 women, low-quality evidence). Two trials (282 women) reported no clear difference between women who received dietary advice versus standard care for pre-eclampsia (low-quality evidence), though fewer women who received dietary advice developed pregnancy-induced high blood pressure (low-quality evidence). There was no clear difference between the groups of women who received low-GI and moderate- to high-GI diet advice, in the number of babies born large-for-gestational age across three trials (777 babies, very low-quality evidence). Only one trial comparing dietary advice with standard care reported on the number of babies who died (either before birth or shortly afterwards), with no deaths in this trial. There were no clear differences for most of the other outcomes assessed in the trials comparing dietary advice with standard care, including caesarean section, perineal trauma, and child skin-fold thickness at 6 months. However, women who received dietary advice gained less weight during their pregnancy across five trials (1336 women) (low-quality evidence). Similarly, there were no clear differences for other outcomes assessed in the trials comparing low- and moderate- to high-GI diet advice, including for caesarean birth and weight gain in pregnancy. The trial comparing dietary advice focused on a high-fibre diet with standard advice found no clear differences for any outcomes. The included trials did not report on a large number of outcomes listed in this review, including outcomes relating to longer term health for the women and their babies (as children and adults), and the use and cost of health services. What does this mean? Dietary advice interventions for pregnant women may be able to prevent GDM. Based on current trials, however, conclusive evidence is not yet available to guide practice. Further large, well-designed, randomised controlled trials are required to assess the effects of dietary interventions in pregnancy for preventing GDM and improving other health outcomes for mothers and their babies in the short and long term. Five trials are ongoing, and four await classification (pending availability of more information) and will be considered in the next update of this review.


Review question: Does feeding preterm infants formula enriched with extra nutrients versus standard formula (designed for term infants) after hospital discharge increase growth rate and improve development? Background: By the time preterm infants are ready to go home from the hospital after receiving care since birth, many are smaller and weigh less than they would have had they stayed in the womb instead of being born early. It may be that feeding preterm infants a formula enriched with extra nutrients (rather than standard formula used to feed term infants) helps them grow more quickly (and catch up with infants born at term) while improving their development. Study characteristics: We identified 16 eligible trials enrolling a total of 1251 infants through searches updated to 8 September 2016. Key findings: These trials provide moderate-quality evidence that unrestricted feeding with nutrient-enriched (vs standard) formula does not have important effects on growth and development up to about 18 months of age. Long-term growth and development have not yet been assessed. Conclusions: Current recommendations to prescribe nutrient-
enriched formula for preterm infants after hospital discharge are not supported by available evidence.

**Commentary**


This position paper considers different aspects of complementary feeding (CF), focusing on healthy term infants in Europe. After reviewing current knowledge and practices, we have formulated these recommendations: **Timing:** Exclusive or full breast-feeding should be promoted for at least 4 months (17 weeks, beginning of the 5th month of life) and exclusive or predominant breast-feeding for approximately 6 months (26 weeks, beginning of the 7th month) is a desirable goal. Complementary foods (solids and liquids other than breast milk or infant formula) should not be introduced before 4 months but should not be delayed beyond 6 months. **Content:** Infants should be offered foods with a variety of flavours and textures including bitter tasting green vegetables. Continued breast-feeding is recommended alongside CF. Whole cows’ milk should not be used as the main drink before 12 months of age. Allergenic foods may be introduced when CF is commenced any time after 4 months. Infants at high risk of peanut allergy (those with severe eczema, egg allergy, or both) should have peanut introduced between 4 and 11 months, following evaluation by an appropriately trained specialist. Gluten may be introduced between 4 and 12 months, but consumption of large quantities should be avoided during the first weeks after gluten introduction and later during infancy. All infants should receive iron-rich CF including meat products and/or iron-fortified foods. No sugar or salt should be added to CF and fruit juices or sugar-sweetened beverages should be avoided. Vegan diets should only be used under appropriate medical or dietetic supervision and parents should understand the serious consequences of failing to follow advice regarding supplementation of the diet. **Method:** Parents should be encouraged to respond to their infant’s hunger and satiety queues and to avoid feeding to comfort or as a reward.

**BNF COMMENT:** This position paper on complementary feeding is an update to ESPGHAN's 2008 paper on the same topic. The recommendations are non-mandatory and targeted at infants living in Europe. New guidance is provided on introduction of allergenic foods including peanuts and gluten, appropriate types of complementary foods, vegan diets, and methods of feeding. Other organisations are also in the process of updating guidelines on complementary feeding. A report by SACN on feeding infants in the first year is soon to be published in the UK and an update to the Department of Health's guidance in this area will follow. Also, EFSA has begun work on the review of its guidance on timing of introduction of complementary feeding, which will inform EU regulation and guidance in the area, and the results are expected in late 2018 (see News section).


Complementary feeding (CF), which should begin after exclusive breastfeeding for 6 months, according to the World Health Organization (WHO), or after 4 months and before 6 months according to the European Society for Pediatric Gastroenterology
Hepatology and Nutrition (ESPGHAN), is a period when the infant implicitly learns what, when, how, and how much to eat. At the onset of CF, the brain and the gut are still developing and maturing, and food experiences contribute to shaping brain connections involved in food hedonics and in the control of food intake. These learning processes are likely to have a long-term impact. Children's consumption of fruit and vegetables (FV) is below recommendations in many countries. Thus, it is crucial to establish preferences for FV early, when infants are learning to eat. The development of food preferences mainly starts when infants discover their first solid foods. This narrative review summarises the factors that influence FV acceptance at the start of the CF period: previous milk feeding experience; timing of onset of CF; repeated exposures to the food; variety of foods offered as of the start of the CF period; quality and sensory properties of the complementary foods; quality of the meal time context; and parental responsive feeding.
News

Policy related

Codex


Codex is the FAO/WHO body that sets global trading standards for food. The Codex Committee on Nutrition and Foods for Special Dietary Uses considered a number of agenda items at its 38th meeting, including an extensive discussion of the Codex Standards for Follow-Up Formula; see meeting minutes for details.

Committees of Advertising Practice (CAP)

New rules ban the advertising of high fat, salt and sugar food and drink products in children’s media (http://bit.ly/2ko4eQL) (December 2016)

It has been announced that rules banning advertising of high fat, salt or sugar (HFSS) food and drink products in TV content targeted at children will now apply to non-broadcast media, including print, cinema and social and online media. The rules, which will apply in media targeted at under-16s, will come into effect on 1 July 2017.

Department of Health Northern Ireland

Northern Ireland Health Minister, Michelle O’Neill, announces plans for legislation to protect mothers breastfeeding in public (http://bit.ly/2k74lUt) (January 2017)

European Food Safety Authority (EFSA)


EFSA has announced that erucic acid, a contaminant which occurs naturally in vegetable oil (particularly rapeseed oil), is a possible health risk for children up to the age of 10 years who consume high amounts of foods containing the substance, such as pastries, cakes, biscuits and infant/follow-on formulæ.


The Panel on Dietetic Products, Nutrition and Allergies (NDA) has confirmed a Population Reference Intake (PRI) for thiamine of 0.1 mg per megajoule of energy requirements for all population groups older than 7 months. The NDA Panel found that in the absence of new scientific data, the value originally set in 1993 by the Scientific Committee for Food does not require changing.


EFSA has launched a public consultation on its draft scientific and technical guidance for applications relating to infant and/or follow-on formula manufactured from protein hydrolysates. Interested parties are invited to submit written comments by 3 March 2017.
Public consultation: follow-on formulae with a protein content of at least 1.6 g/100 kcal ([http://bit.ly/2iFkCzK](http://bit.ly/2iFkCzK)) (January 2017)
EFSA has launched a public consultation on its draft Scientific Opinion on the safety and suitability for use by infants of follow-on formulae with a protein content of at least 1.6 g/100 kcal. Interested parties are invited to submit written comments by 3 March 2017.

EFSA has launched a public consultation on its draft scientific opinion on dietary reference values for vitamin K. Dietary reference values for vitamin K for adults, infants, children, and pregnant and lactating women are proposed. Interested parties are invited to submit written comments by 24 February 2017.

The protocol for EFSA's systematic review on the health effects of age of introduction of complementary feeding will be opened for public comment later this year and EFSA's draft Scientific Opinion on the appropriate age of introduction of complementary foods, based on the outcome of the systematic review, will be opened for public comment in 2018.

BNF COMMENT: EFSA’s Scientific Opinion (2009) that introducing complementary feeding between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects for infants in the EU is currently under review. Any changes to this Scientific Opinion will have implications for EU laws relating to foodstuffs intended for infants and young children. The European Commission Directive (2006) on processed cereal-based foods and baby foods for infants and young children currently legislates that the stated age for which a baby food product is appropriate for use shall not be less than 4 months. This law is applied in the UK, where it is permitted to advertise certain baby food products as suitable from 4 months of age, despite the recommended age of complementary feeding in the UK being 6 months (this is currently being reviewed by SACN in its review of the UK complementary feeding guidelines; the report is scheduled for publication in 2017). It is anticipated that UK food legislation will continue to follow EU rulings after the UK leaves the EU and therefore any changes to EU laws about appropriate age of complementary feeding will likely affect the marketing of baby food products in the UK.

Food Standards Agency advisory committees

- **Committee on Toxicity (COT)**
  COT has assessed the possible health risks to infants and young children arising from acrylamide exposure from different dietary sources. For breast-fed infants this risk in terms of cancer was deemed to be low but for formula fed infants and infants and young children eating solid foods, potentially there is cause for concern. However, it was concluded that currently the available scientific information does not allow quantification of any risk. This information will be considered by SACN in its review of complementary feeding guidelines.
COT statement on arsenic in the diets of infants and young children (http://bit.ly/2iWRJxG) (December 2016)
COT considered the possible risks to infants and young children from exposure to inorganic arsenic from different dietary sources. For infants aged 0-4 months old who are fed only on breast milk, ready-to-feed formula, or powder formula made with water containing typical inorganic arsenic concentrations, exposures were considered of low concern. However, COT concluded that there could be a small risk when powder formula is prepared with water containing inorganic arsenic at the upper end of the concentration range in public water supplies. Similarly, with the introduction of complementary feeding, there could be a small risk for some older infants and young children, particularly when water contains higher levels of inorganic arsenic. Based on the findings of the report, COT recommends that the advice not to use rice drinks as a substitute for breast milk, infant formula or cows’ milk should stay in place. This information will be considered by SACN in its review of complementary feeding guidelines.

Addendum to the 2015 COT Statement on potential risks from hexabromocyclododecanes (HBCDDs) in the infant diet (http://bit.ly/2iO6bEB) (November 2016)
COT has reviewed its statement on HBCDDs as new data has become available. The conclusion of this review is that the margins of exposure to HBCDDs by dietary intake of breast milk, infant formula, commercial infant food and fish oil are not a cause for concern for any age group. This information will be considered by SACN in its review of complementary feeding guidelines.

COT meeting (http://bit.ly/2jwDgHa) (December 2016)
Agenda items at the meeting included the potential risks from vitamin A, iodine and nickel in the diets of infants and children aged up to 5 years and the COT draft statement on maternal and infant dietary exposures and risk of development of atopic outcomes and autoimmune disease.

The Advisory Committee on Novel Foods and Processes (ACNFP)
ACNFP is considering an application to extend the food categories to which docosahexaenoic acid (DHA) rich oil from schizochytrium can be used in the European Union (EU) as a food ingredient (http://bit.ly/2jPUf7I) (January 2017)
Mara Renewables Corporation is seeking to extend the food categories (to include fruit and vegetable purees, infant formula, other foods for special groups and baby foods) in which this novel food ingredient can be used as an alternative source of DHA rich oil.

HM Government
A Bill to control the advertising and promotion of feeding products for babies and children has passed the first reading at the House of Commons under the Ten Minute Rule. The Bill is to establish arrangements to set standards for the efficacy of products and to measure claims against those standards; to make provision about penalties for
advertisers and promoters who do not meet the standards; and for connected purposes. This Bill is expected to have its second reading debate at the House of Commons on 24 February 2017.


The Commons Committee Select held a meeting to take stock on how implementation of the National Maternity Review, including the need for improved support in breastfeeding, is progressing.

**International Baby Food Action Network (IBFAN) World Breastfeeding Trends Initiative (WBTi)**


WBTi has published the report *Has Your Nation Done Enough to bridge gaps?* on the global status and progress of implementation of the Global Strategy for Infant and Young Child Feeding 2008-2016 ([http://bit.ly/2jU6P5z](http://bit.ly/2jU6P5z)). A WBTi report on infant feeding policies, programmes and practices in the UK has also been published ([http://bit.ly/2f0rgM](http://bit.ly/2f0rgM)). The report found that out of the 84 countries assessed, the UK was ranked as 58th for its policy, programmes and practices on infant and young child feeding.

**Scientific Advisory Committee on Nutrition (SACN)**

*Minutes from SACN’s third main meeting of 2016 have been published* ([http://bit.ly/2iSW2GV](http://bit.ly/2iSW2GV)) (January 2017)

The main SACN group held its last meeting of 2016 in November and several items in the minutes are relevant to infant feeding. It was reported that, in relation to cancellation of the Infant Feeding Survey (IFS), the SACN Subgroup on Maternal and Child Nutrition (SMCN) will be reviewing information from DH about how some of the data collected in the IFS might be built into the Maternal and Child Data Set. It is hoped this information will be made available for the next SMCN meeting, scheduled for 28 February 2017. An update was provided on the work of SMCN. Professor Angus Walls, an expert in oral health, has recently joined SMCN and Dr Anthony Williams has stood down as Chair. SMCN has reviewed SACN’s comments on the complementary feeding report and a number of amendments have been made to recognise comments of SACN members. The SMCN drafting group met on 21 November 2016 to produce a final version of the complementary feeding report. A chapter on oral health has been added, based on a paper provided by Dr Jenny Godson, Consultant in dental health at PHE. The next SACN main meeting will be held on 16 March 2017.

**United Nations (UN)**


A joint statement by the UN Special Rapporteurs on the Right to Food, Right to Health, the Working Group on Discrimination against Women in law and in practice, and the Committee on the Rights of the Child has been issued in support of increased efforts to promote and support breastfeeding.
Guidelines

Department of Health (DH)


This guidance from DH gives step-by-step support for businesses on developing a front-of-pack nutrition label. New information added to the report includes advice on providing consistent communication to consumers on how to use the front-of-pack nutrition labelling in choosing a healthy balanced diet and clarification on how the voluntary scheme complies with existing legislation.

Public Health England (PHE)


New research conducted by PHE, with nutritional analysis by the British Nutrition Foundation, indicates that children are consuming half their daily recommended sugar intake at breakfast. A new ‘Be Food Smart’ app for parents has been developed by PHE to highlight just how much sugar, saturated fat and salt can be found in everyday food and drink that children are consuming.

United Nations Children’s Fund (UNICEF)


This UNICEF UK Baby Friendly Initiative information sheet explains responsive feeding in relation to breast milk and formula milk and how this feeding practice can benefit infants and their parents.

World Health Organization (WHO)


This guideline provides global, evidence-based recommendations on the use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6–23 months and children aged 2–12 years.

Research funding

Innovate UK


This project, led by Ella’s Kitchen and the University of Reading, is to develop a range of baby and toddler food products with lowest in market sugar contents and innovative textures, with the aim of improving the health of young children by offering better, more nutritional choices at mealtimes.
Other news

British Nutrition Foundation (BNF)
This year's BNF Healthy Eating Week will take place on 12-16 June 2017 and nurseries, schools, universities and workplaces are all invited to take part. Registration only takes a few minutes and means you will be the first to hear about plans for BNF Healthy Eating Week 2017 and have access to resources to help you plan activities for your Week.

Children’s Food Trust
This report describes findings from a survey of 2001 parents about their practices and attitudes relating to child feeding. It also explores current issues and research in the area of child feeding. An update to the menus in the Children’s Food Trust’s ‘Voluntary Food and Drink Guidelines for Early Years Settings in England – A Practical Guide’ is anticipated in the first quarter of 2017.

Department of Health (DH)
DH has launched a new website to update the public on the government’s ongoing work to reduce childhood obesity.

Case studies describing the progress being made across the country by local authorities and businesses to improve children's nutrition, health and wellbeing have been published by the Department of Health.

Nestle
This new resource for Healthcare Professionals explores what is responsive feeding and how it can benefit infants.

NHS Digital (formerly the Health and Social Care Information Centre)
NHS Digital has published the latest findings from the government’s National Child Measurement Programme for England for the 2015/2016 school year, providing data on the weight of Reception (aged 4-5 years) and Year 6 (aged 10-11 years) children. Over a fifth of Reception children were overweight or obese, increasing to over a third in Year 6. The prevalence of obesity has increased since 2014/2015 in both age groups.

NHS Digital has published data from the 2015 Health Survey for England, which describes prevalence of health conditions, including overweight and obesity, and risk factors for disease in children (aged 2 years and older) and adults living in England.
Public Health England
This report describes breastfeeding prevalence at 6-8 weeks after birth in the months July – September 2016 for England. Prevalence is reported as 44.4% (95% Confidence Interval: 44.2 – 44.6%), this compares to 43.1% for Quarter 2 2015/16.

Royal College of Paediatrics and Child Health (RCPCH)
The RCPCH State of Child Health report brings together data for the first time on a comprehensive list of 25 measures of the health of UK children, ranging from specific conditions such as diabetes, risk factors for poor health such as obesity and a low rate of breastfeeding, to child deaths. The report includes recommendations on ways to improve the health of children in the UK.

Scottish Government

Scotland’s baby box scheme has started (http://bit.ly/2iSxxd0) (January 2017)
Baby boxes containing essential items, such as clothes, nappies and books, and the box itself that can be used as a bed, are being given to expectant mothers in Scotland in order to give babies the best start in life and encourage parents to engage with antenatal and postnatal services. The baby box scheme will be rolled out to all newborns in Scotland by the summer of 2017.

It has been announced that more teachers and graduates are to be recruited for nurseries in deprived areas of Scotland through a £1.5 million investment to expand early learning and childcare services.
## Conferences

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