Scientific Advisory Committee on Nutrition

Draft Feeding in the First Year of Life Report

Scientific consultation: 19 July to 13 September 2017

Contents

Chapter 1. Introduction

1. There has been no comprehensive risk assessment of infant and young child feeding in the UK since the Committee on Medical Aspects of Food Policy (COMA) published its report 'Weaning and The Weaning Diet' in 1994.

2. A number of recommendations made by the Scientific Advisory Committee on Nutrition (SACN) and by international expert committees since the COMA 1994 review have carried implications for current infant feeding policy (for example, adoption of World Health Organization (WHO) Growth Standards (WHO MGRS 2006a, 2006b; SACN/RCPCH 2007) and revisions to energy requirements (FAO, 2004; SACN, 2011)).

3. Accordingly SACN requested its Subgroup on Maternal and Child Nutrition (SMCN) to review recent developments in this area. To complement this work, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) was asked by the Department of Health (DH) to conduct a review of the risks of toxicity from chemicals in the infant diet, and examine the evidence relating to the influence of the infant diet on development of food allergy, and atopic and auto-immune disease.

Terms of Reference

4. The terms of reference for the review were:

   a) To review the scientific basis of current recommendations for complementary and young child feeding up to 5 years (60 months) of age. This interim draft covers infants aged 0-12 months.
   b) To consider evidence on developmental stages and other factors that influence eating behaviour and diversification of the diet[1] in the early years.
   c) To review the nutritional basis for current dietary recommendations applying to breastfeeding mothers (where relevant to the health of the infant)
   d) To make recommendations for policy, practice and research.

5. In keeping with SACN's terms of reference, this review is restricted to risk assessment and only healthy term infants have been considered.

6. Breastfeeding represents the physiological norm for infant feeding and 80% of UK infants are now at least initially breastfed[2]. Consequently, the role, timing and

[1] *Diversification* of the diet refers to the progression from an exclusively milk-based diet to an eating pattern which includes a wide range of foods.

type of complementary feeding can only be considered within the context of their potential benefits balanced against the risk of displacing breast milk. The review therefore also considers the accumulated evidence on the optimal duration of exclusive breastfeeding.

Key outcomes

7. This document aims to summarise and evaluate the implications of current evidence to the UK context to enable risk managers to assess the appropriateness of current infant feeding advice.

8. Growth is a sensitive measure of both nutrient deficiency and nutrient excess; there is also increasing understanding of the relationship between patterns of early growth and health risks in later life (SACN, 2011). Currently there is consensus that the pattern of growth associated with least risk of both current and long-term ill-health is that defined by the WHO Growth Standard which the United Kingdom adopted in 2007 for the purpose of clinical and population growth monitoring (SACN, RCPCH, 2007). The current report thus regards achievement of the growth pattern described by the WHO Standard as a key indicator of health.

9. Infectious illnesses, particularly of the gastrointestinal and respiratory tracts are leading causes of infant morbidity and mortality both globally and in the United Kingdom. Feeding practices in infancy have an important bearing on the risk of such illnesses. The current report set out to quantify the magnitude of these risks and place them in the context of variation in infant feeding practices, in particular the effect of not breastfeeding exclusively for around the first six months of life and the timing of introducing complementary foods to the infant.

10. Not breastfeeding is associated with certain health consequences for the mother. This report sought to quantify the extent of these consequences in the context of changes in the incidence, prevalence and duration of breastfeeding in the United Kingdom.

11. The second half of infancy (6-12 months), leading into the second year of life is a challenging period nutritionally. Widening the range of foods accepted introduces particular considerations about the energy and nutrient density of the diet, its macronutrient balance, and the adequacy of micronutrient balance. Demands vary as the infant grows and levels of physical activity increase with the development of independent mobility. There may also be short-term variation in

[2] Incidence of breastfeeding is defined as the proportion of babies who were breastfed initially. This includes all babies who were put to the breast at all, even if this was on one occasion only. It also includes giving expressed breastmilk to the baby.

nutrient demands, for example associated with intercurrent illness, anorexia and subsequent catch-up growth. Allowance must be made when reviewing nutrient requirements.

12. Infant feeding is an activity involving both the dependent child and a caregiver. This relationship evolves during the early years of life until a point is reached at which the child is able to eat independently. The nature of this relationship is a key determinant of the child's nutritional intake. What the child needs may not always match the caregiver's perceptions; the way in which food is offered or administered has to take account of the individual child's developmental progression which is particularly rapid in the first year; the way in which food is offered or administered, and the age at which foods are presented, may also modify acceptance and either help or hinder diversification of the diet, perhaps with long-term implications for eating behaviour. Accordingly the report also set out to summarise evidence from the field of behavioural psychology on food acceptance in the early years.

13. Oral health is part of general health and wellbeing and contributes to the development of a healthy child. Tooth decay is the most common oral disease affecting children and yet it is largely preventable. Infant and complementary feeding practices are among the many factors influencing oral health, and the evidence on the association between feeding in the first twelve months of life and oral health is therefore considered in this report

14. Allergy to food constituents is an increasing cause of ill-health in children and adults. Its origins are unclear; a number of environmental factors may be operative, including lack of exposure to breastmilk, but it is speculated that the timing of exposure to food antigens in early life may modify the development of immune tolerance to food constituents. The COT was asked by the Department of Health (DH) to evaluate in collaboration with SACN the relevant evidence on this topic. This evidence has been separately reported by the COT though the Food Standards Agency (FSA) in a series of COT Statements. A joint SACN:COT working group was established to consider the findings from the COT statement on the timing of introduction of potentially allergenic foods, in light of the current SACN review on feeding in the first year of life (see Chapter 11).

15. Infants proportionately have a high food intake per unit of body weight. This can expose them to relatively greater intakes of environmental food contaminants, notably some metals and persistent organic pollutants, than other population sectors. The COT was asked by DH to evaluate in collaboration with SACN the relevant evidence on this topic. This evidence has been separately reported by the COT though the FSA.

Chapter 2. Policy background

History of UK recommendations

16. Over the last fifty years there have been significant changes to United Kingdom infant feeding policy and practice.

17. During the 1970s there was particular concern about excessive weight gain in infancy (Taitz, 1971; Shukla et al., 1972) and the high incidence of infantile hypernatraemic dehydration, either in an isolated form or associated with acute gastroenteritis (Taitz and Byers, 1972; Davies, 1973; Chambers and Steel, 1975). These conditions were linked to early use of cows' milk, errors in the reconstitution of infant formula, and early introduction of solid foods (Wilkinson et al., 1973), often within the first few weeks of life.

18. Accordingly, in 1974, a Working Party set up by the Committee on Medical Aspects of Food and Nutrition Policy (COMA) considered infant feeding practices and recommended breastfeeding for a minimum of two weeks, preferably for the first four to six months of life. It strongly discouraged the introduction of solid foods before four months of age and made recommendations about vitamin supplementation, highlighting the need for further research.

19. Following these recommendations, the Department of Health and Social Security commissioned a nationally representative survey of infants born in England, Wales and Scotland in September and October 1975 (Martin, 1978). In 1980, a further sample of infants born in England, Wales and Scotland during August and September in 1980 were surveyed. These surveys showed that the percentage of infants who were breastfed (i.e. ever put to the breast) increased from 51% in 1975 to 67% in 1980. Moreover the proportion of infants receiving solids before three months of age fell from 85 to 55 percent.

20. A further Working Party (Department of Health and Social Security, 1980) endorsed the recommendations made by the previous report in relation to breastfeeding and advised that the introduction of complementary foods should be no later than six months (see Table2.1). It also reviewed evidence on gluten sensitisation and stated that for the majority of infants there was no evidence that wheat-based cereals posed a risk. For the potentially allergic child, the Working Party advised that it is reasonable to avoid early introduction of foods that are commonly considered allergenic. As the child gets older a greater diversity of foods can be cautiously introduced until an unrestricted diet can be achieved.

21. A third report of the Working Party on practices in infant feeding (Department of Health and Social Security, 1988) reaffirmed earlier recommendations and endorsed conclusions of the 1980 report in relation to allergens in complementary foods and vitamin supplementation. In addition, the Working Party stated that a dietitian’s expert advice was essential if dietary restriction was considered in relation to foods commonly considered allergenic.

22. In 1991, COMA set up a Working Group to review the scientific evidence in relation to nutritional adequacy of the weaning diet. While previous “Present day practice” reports addressed the diet of infants in the first months after birth, “Weaning and the Weaning Diet” (Department of Health, 1994) included recommendations on when to wean, type of first foods to introduce and the progression of infant feeding (see Table 2.1). The report endorsed breastfeeding for the first four to six months of life, followed by the introduction of non-wheat cereals, fruit, vegetables and potatoes as suitable first weaning foods. It recommended delaying the introduction of potentially allergenic foods (for example, eggs, nuts and wheat) until six months at the earliest. Earlier recommendations on vitamin supplementation were revised to state that from the age of six months, infants receiving breast milk as their main drink, or less than 500 ml/ day of infant formula, should be given supplements of vitamins A and D.

23. In 1999, COMA undertook a review of the Welfare Food Scheme (DH, 2002). Based on recommendations made by COMA, the Scheme (which had been in place since 1940) was changed in a number of respects and re-designated “Healthy Start”. Important aspects were the obligation for beneficiaries to register during pregnancy with a health professional (thus enabling nutrition counselling), widening of the range of foods offered through the introduction of exchangeable vouchers, and reformulation of the vitamin preparations as “Healthy Start” vitamin supplements for young children and mothers. Healthy Start replaced the means tested elements of the Welfare Food Scheme throughout the UK in 2006.

World Health Organization recommendations

24. In 1979, a joint meeting was held with participants from government, non-governmental organisations, the United Nations system, the infant food industry and scientists to discuss recommendations for infant and child feeding. The outcome, published by the World Health Organization (WHO) and UNICEF, was to recommend the introduction of complementary foods at around four to six months of age (see Table 2.2).

25. The WHO published guidelines in relation to infant and child feeding specifically for the European region in 2003 (see Table 2.2). These recommended the introduction of complementary foods at six months of age, acknowledging that

some infants may need complementary foods earlier, though not before four months of age. Recommendations about the type and consistency of first solid foods were also made.

26. In 2001 the WHO and Pan American Health Organization published guiding principles for complementary feeding of the breastfed child (see Table 2.2). These were followed in 2004 by principles for complementary feeding of the non-breastfed child. Both reports recommended the introduction of complementary foods at six months of age.

27. The most recent recommendations for complementary feeding published by the WHO in 2013 have not differed from the 2003 and 2004 guidance following a systematic review of the scientific evidence (see Table 2.2).

UK guidance on the duration of exclusive breastfeeding and infant feeding

28. Since 2001 the WHO has recommended that mothers worldwide exclusively breastfeed infants for the first six months to achieve optimal growth, development and health (WHO, 2001). Thereafter, they should be given nutritious complementary foods as breastfeeding continues up to the age of two years or beyond. These guidelines were reiterated in the WHO's Global Strategy (WHO, 2003)

29. "Exclusive breastfeeding" is defined as feeding only breastmilk. No other liquids have been given, though administration of medicines, vitamin drops and oral rehydration solution is permitted.

30. In 2001 the Scientific Advisory Committee on Nutrition (SACN) endorsed the WHO's recommendation of exclusive breastfeeding for the first six months of an infant's life. SACN advised:

> *"That there is sufficient scientific evidence that exclusive breastfeeding for six months is nutritionally adequate. However the group[3] noted that early introduction of complementary foods is normal practice in the UK and that mothers do this for many valid personal, social and economic reasons."*

[3] The *Ad hoc* Expert Group on Child and Maternal Nutrition which was convened in December 2000 under the Chairmanship of Professor Alan Jackson in light of the WHO activity on the optimal duration of breastfeeding. The *Ad hoc* Group included members of the former Committee on Medical Aspects of Food Policy (COMA) panel on Child and Maternal Nutrition.

SACN therefore recommended that there should be some flexibility in the advice, but that any complementary feeding should not be introduced before the end of four months (17 weeks).

31. Historically the terms "weaning foods" or "solids" were commonly used to describe the foods introduced to infants alongside breastmilk (or infant formula). In this report the term "complementary foods" has been used to indicate that the purpose of introducing foods other than breastmilk is to diversify the diet whilst breastfeeding continues during the early year of life, not to "wean" the infant from the breast. In the UK literature "complementary food" usually implies the solid food component of the infant diet but the WHO definition would include liquid complementary foods such as infant formula (WHO, 2007)

UK policy recommendations at the time of writing (2016)

32. In England and Wales, infant feeding guidance from the Department of Health (DH), which reflects current infant feeding policy, is published on the NHS Choices website 'Your pregnancy and baby guide'[4]. This is regularly reviewed by officials in the relevant government organisations (principally, Health Departments and the Foods Standards Agency) and updated when policy and/or advice changes. Additional consumer-facing advice on infant feeding, the introduction of solid foods into an infant's diet and establishing healthy eating behaviours for young children is provided on the Start4Life website (www.nhs.uk/start4life). Public Health England has also produced the resource *'Health matters: giving every child the best start in life'* for health professionals and local authorities with the aim of increasing the proportion of children ready to learn at two years and ready for school at five years through investment in early years services[5]. Public Health Wales provides further information and resources on infant feeding through its website, Health Challenge Wales[6].

33. In 2011, the Scottish Government published 'Improving Maternal and Infant Nutrition: A Framework for Action'[7], a ten year action plan with the overarching goal of ensuring that all children in Scotland have the best possible start to life, are ready to succeed and live longer, healthier lives. To support this Framework, The Scottish Government has created its FeedGood website[8] on infant feeding choices and a number of other consumer and professional resources on breastfeeding, introducing solids, and nutritional guidance and food standards have been developed by NHS Health Scotland (www.healthscotland.com).

[4] http://www.nhs.uk/conditions/pregnancy-and-baby/pages/pregnancy-and-baby-care.aspx
[5] https://www.gov.uk/government/publications/health-matters-giving-every-child-the-best-start-in-life/health-matters-giving-every-child-the-best-start-in-life
[6] www.healthchallengewales.org/infantfeeding-publications
[7] http://www.gov.scot/Publications/2011/01/13095228/0
[8] http://www.feedgood.scot/

34. In Northern Ireland, infant feeding policy guidance is provided by the Department of Health Northern Ireland, and in 2004 a statement on the introduction of solids was issued outlining new recommendations on breastfeeding duration and complementary feeding within a Chief Medical Officer circular[9]. In 2013, the Northern Ireland Breastfeeding Strategy – Breastfeeding a Great Start[10] was launched providing a framework for promoting and supporting breastfeeding. To support best practice, the Public Health Agency (PHA) for Northern Ireland gives all parents a number of key publications in hard copy[11] which are updated by PHA on an annual basis.

35. At the request of the Department of Health in England, the National Institute for Health and Clinical Excellence (NICE) has also produced public health guidance aimed at improving the nutrition of pregnant and breastfeeding mothers and children in low-income households (NICE guidelines [PH11]: Maternal and child nutrition). In particular, this guidance addresses disparities in the nutrition of low-income and other disadvantaged groups compared with the general population[12].

36. Recommendations advise exclusive breastfeeding for around the first six months of the infant's life; breastmilk should continue to be given as the main drink alongside appropriate complementary foods for as long as the mother wishes. Infant formula meeting the compositional requirements of EU legislation should be used as an alternative when mothers choose not to breastfeed or choose to supplement breast milk. Guidance regarding the safe preparation, storage and handling of infant formula should always be followed. Other milks or milk substitutes, including cows' milk, should not be introduced as a main drink until 12 months of age. After this cows' milk should be whole (not semi-skimmed) milk until at least two years of age.

37. It is currently recommended that all children aged from six months to five years of age should be given vitamin supplements containing vitamins A (233µg) and C (20mg). This is a precautionary measure, to ensure that requirements are met, when it is difficult to be certain that the diet provides a reliable source. In order to reduce the risk of excessive vitamin A consumption formula-fed infants should not be given vitamin supplements if they consume more than 500ml infant formula per day.

38. It is also recommended that infants from birth to one year of age be given a daily supplement containing 8.5 to 10µg of vitamin D. Infants fed infant formula should not be given a vitamin D supplement until they are having less than 500ml infant

[9] http://www.dhsspsni.gov.uk/hssmd_breastfeeding.pdf
[10] https://www.health-ni.gov.uk/publications/breastfeeding-strategy
[11] www.publichealth.hscni.net/publications
[12] https://www.nice.org.uk/guidance/ph11

formula per day (SACN, 2016). This represents a change from previous advice which was based on the assumption that maternal vitamin D supplementation during pregnancy and then the vitamin D consumed from breast milk would provide the infant with adequate vitamin D for the period of exclusive breastfeeding. The few available data suggest that it is unlikely that an exclusively breastfed infant in the UK would maintain a serum 25(OH) D concentration ≥ 25 nmol/L for six months (SACN, 2016).

39. Advice on the introduction of allergenic foods into the infant diet is based on recommendations from ‘Weaning and the Weaning diet’ (COMA, 1994):

> *“Where there is a family history of atopy or gluten enteropathy, mothers should be encouraged to breastfeed for six months or longer. Weaning before four months should particularly be discouraged and the introduction of foods traditionally regarded as allergenic should be delayed until six months at the earliest”*”

40. It is recommended that allergenic foods, such as peanuts, nuts, seeds, egg, cows’ milk, soya, wheat (and other cereals that contain gluten, for example, rye and barley), fish and shellfish, should be introduced into the infant’s diet in very small amounts and one at a time, watching carefully for any symptom of an allergic reaction. Where parents offer complementary foods before six months of age, it is advised that commonly allergenic foods are avoided until the infant is six months old.

41. In 2016, the government in England published ‘Childhood Obesity - A Plan for Action’ (HM Government, 2016) which aims to significantly reduce England’s rate of childhood obesity by 2026. The Plan includes a sugar reduction pledge to reduce sugar by 20% in products commonly consumed by children by 2020. The sugar reduction programme will also work to reduce the sugar content of product ranges explicitly targeted at infants and young children.

Chapter 3. Methodology

Sources of evidence

42. The SACN *Framework for the Evaluation of Evidence* (SACN, 2012)[13] was applied to identify and select suitable evidence. Consideration of the evidence published to the end of 2015 was mainly restricted to prospective cohort studies, and randomised controlled trials (RCTs) where these were available, but cross sectional studies and case reports were also considered where these informed interpretation of the evidence. Consideration was focused on, but not limited to, studies conducted in settings of direct relevance to the United Kingdom. Only studies published in the English language were considered.

43. Where applicable, previously published SACN reports[14] were considered and searches made to update evidence that may have accrued since publication. Findings from a number of Statements from the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) examining the risks of toxicity from chemicals in the diet of infants which were conducted to complement the SACN review, are summarised in Chapter 11.

44. A number of different search strategies were employed to identify literature for consideration. Published systematic reviews such as the Cochrane Review 'Optimal Duration of Exclusive Breastfeeding' (Kramer and Kakuma, 2012) and the US Agency for Healthcare Research and Quality Evidence Report/Technology Assessment on 'Breastfeeding and Maternal and Infant Health Outcomes in Developed Countries' (Ip et al., 2007) represented key sources but other systematic reviews were also identified and are cited in relevant chapters of this report. In each case supplemental searches were conducted using PubMed to cover the ensuing time period, allowing for overlap to include any studies that may have been published during preparation of the reviews. Additional studies were identified by hand searches. Expert advice and information and recommendations from grey literature have also informed the review. Peer review of Chapter 8 was undertaken by an external expert, Dr Lucy Cooke.

---

[13] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/480493/SACN_Framework_for_the_Evaluation_of_Evidence.pdf

[14] SACN reports on: Salt and health, 2003; Review of dietary advice on vitamin A, 2005; Iron and health, 2010; Dietary Reference Values for energy, 2011; The influence of maternal, fetal and child nutrition on the development of chronic disease in later life, 2011; Vitamin D and Health, 2016. Joint SACN/RCPCH report on: Application of WHO growth standards in the UK, 2007.

45. Chapter 9 provides a review of the evidence on the influence of infant feeding practices on the development of early childhood caries and malocclusion. A literature search was conducted using Ovid MEDLINE to identify the most recent systematic reviews of relevance to the UK population and which included evidence judged to be of sufficient quality. Individual studies were also considered where systematic reviews were not available or did not fully address the questions posed.

46. Two large national Surveys informed the sections describing current infant feeding practice in the United Kingdom (Chapter 10). These were the Infant Feeding Survey 2010 (McAndrew et al., 2012) and the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) 4 – 18 months of age (Lennox, 2013).

Issues requiring consideration in relation to infant feeding evidence

47. It is well recognised that different types of evidence must be adduced to inform public health policy, particularly in the area of nutrition (SACN, 2012)[15].

48. Randomised controlled trials (RCTs), if properly conducted and designed, provide the best evidence on the relationship between an exposure and health outcome (Horta & Victora, 2013). RCTs are designed to minimise the risk of confounding as participants differ only in the randomised treatment or exposure (SACN, 2012) and the validity of the evidence may be increased due to the existence of standards for conducting, analysing and reporting RCTs (Schulz et al., 2010). Their generalisability, however, may be limited and it is usually not possible to blind the assessors and participants to the allocation which is often problematic. Additionally, many consider it unethical to allocate healthy infants randomly to a dietary regimen other than exclusive breastfeeding from 0-6 months. Accordingly there are relatively few RCTs in young infants (Cohen et al., 1994; Dewey et al., 1999; Wells et al., 2012) and existing studies were predominantly undertaken in resource-poor settings.

49. An alternative approach has been to allocate parents to an intervention that may increase the prevalence of exclusive breastfeeding (from 0-6 months). A key example of this approach was the Promotion of Breastfeeding Intervention Trial (PROBIT) conducted in the Republic of Belarus in which cluster randomisation was applied to allocate over 17,000 mothers and their infants to a novel intervention (the UNICEF Baby Friendly Hospital Initiative) that might increase both the incidence and prevalence of breastfeeding (Kramer et al., 2001). The cohort arising from PROBIT has subsequently provided informative data on a

[15] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/480493/SACN_Framework_for_the_Evaluation_of_Evidence.pdf

range of breastfeeding-related outcomes, extending from infancy to later childhood.

50. Due to the paucity of RCT data in relation to infant feeding, it is necessary to use additional evidence from observational cohort studies, although the latter cannot be used to infer causation.

51. Measurement of exposure is a further significant problem in relation to infant feeding studies. This particularly relates to the definition of "breastfeeding" and to measuring the age at which interventions of interest are made.

52. Both the duration and the intensity of breastfeeding may vary considerably, even within the same population. Breast milk may be given alone for six months, barely at all in the first week of life, or be combined in varying amounts with breast milk substitutes and other foods. Participants following any of these patterns are sometimes described as *"ever breastfed"* when data are reported. Outcomes in breastfed infants (and mothers who breastfeed) are, however, frequently dose-dependent and will not be adequately demonstrated unless the intensity of exposure is measured.

53. In order to address the inconsistencies and lack of precision in how breastfeeding is described, WHO recommend that standardised definitions should be applied for research and health survey purposes (WHO, 2003).

- "Exclusive breastfeeding" indicates that the infant has received only breastmilk (from the mother or a wet nurse), or expressed breastmilk. No other liquid or solid foods have been given, though drops and syrups containing medicines, mineral supplements or vitamins, and oral rehydration solutions may be given.

- "Predominant breastfeeding" indicates that breastmilk is the main source of nutrition though other liquids (such as drinks, teas or oral rehydration solutions) may be given provided that they are not food-based.

- "Full breastfeeding" is a term often used to describe groups of infants who individually are either exclusively or predominantly breastfed.

- "Partial breastfeeding" or "mixed feeding" describes the use of breastmilk alongside other liquid or solid foods, for example infant formula or "weaning" foods.

54. Even when standard definitions are used consideration must be given to the research context in which data were collected. For example, Demographic Health Surveys may merely describe the pattern of feeding recalled in the last 24-hours (WHO, 2007; WHO, 2010) whereas the UK Infant Feeding Survey

definition of "exclusive breastfeeding" at all infant ages required nothing other than breast milk to have been given since birth (McAndrew, et al., 2012).

55. Patterns of feeding evolve rapidly in infancy and there is considerable variation between individuals, in keeping with the pace and nature of infant development. In this context knowledge of the exact age at which individual participants first encountered exposures of interest is of considerable value. Retrospective collection of such data is unlikely to be accurate, particularly after intervals of months or years. Prospective data collection, sampling at frequent points during the early months of life (for example weekly or at least monthly) is more reliable.

56. Prospective data collection also assists in the detection of reverse causality, a common source of bias in infant feeding studies (Bauchner et al, 1986). For example, infants who are heavier or hungrier may be more demanding and thus be introduced earlier than lighter or more satisfied infants, to foods other than breast milk; potential associations between the subsequent development of obesity in such infants would be confounded in an analysis of incomplete retrospective data. Without accurate measurement of the infant's size or assessment of appetite, links to early feeding could erroneously imply causality (Heinig, 1993; Kramer et al., 2001). Retrospective data collection may also be susceptible to recall bias due to the time lapse when obtaining feeding histories (Horta et al*.,* 2013); parents may be influenced in their reporting by their subsequent experience.

57. In many industrialised societies, such as the United Kingdom, patterns of infant feeding are strongly confounded by socio-demographic factors, such as smoking, parental education, socioeconomic status and family size. Breastfeeding mothers are more likely to be health-conscious, and, therefore, also more likely to promote healthy habits to their children as they grow up, including promotion of physical activity and intellectual stimulation (Horta and Victora, 2013). Information on potential confounding factors should therefore be collected and taken into account in the analysis of study findings. This can be difficult, however, because individual socio-economic measures are unlikely to fully characterise socio-economic status. For example, in the Gateshead Millennium Study three different markers of deprivation or educational level were all independently associated with breastfeeding initiation in a multivariate prediction model, when mutually adjusted (Parkinson et al., 2011). Thus, if only one of these measures was collected there would be residual confounding even after apparent adjustment for socio-economic group.

58. Sometimes it may be useful to consider studies which have examined the links between breast milk exposure and health outcomes in resource-poor countries because socio-demographic determinants of breastfeeding in these settings are

much less apparent or may even operate in the opposite direction to those encountered in the United Kingdom.

59. The extent to which confounding factors have been controlled for varies between studies and is an important consideration when judging the quality of evidence.

60. Where alternatives to breast milk are evaluated, for example in controlled trials, it may be unclear where outcomes directly reflect the intervention or indirectly reflect the lack of breast milk. For this reason it remains important that any trials of breast milk substitutes incorporate a breastfeeding reference group. Preferably this should be contemporaneously studied but, alternatively, reference data may be applied if recruiting a reference group is infeasible (Department of Health, 1996).

Chapter 4. Infant feeding, growth and health

Physiological and developmental influences

61. Maturation of the gastrointestinal, renal and neurological systems influences the infant’s ability to accept foods other than breastmilk or infant formula (WHO, 1998).

Gastrointestinal function

62. During the first year of life, normal luminal digestion and mucosal absorption change considerably, but this may have limited relevance to the efficiency of micronutrient absorption from complementary foods. By six months of age, healthy infants are capable of absorbing sufficient amounts of micronutrients from complementary foods provided that these foods are of adequate nutrient density and do not contain levels of other dietary constituents that interfere with absorption (WHO, 1998).

63. Following birth, the human intestine is rapidly colonised by microbes; factors including gestational age, mode of delivery, infant feeding, sanitation and antibiotic treatment are known to influence colonisation (Adlerberth and Wold, 2009; Marques et al., 2010). The intestinal microbiota of newborn infants is characterised by low diversity, which increases during infancy so that by about two years of age, the microbiota fully resembles that of an adult. Both habitual and acute dietary exposures have been shown to influence composition of the gut microbiota (Claesson et al., 2012), and the health impact of these compositional changes remains under investigation.

64. Diet plays a major role in the development of the microbiota during infancy; breastfed infants are exposed to the milk microbiome which has been reported to contain more than 700 species of bacteria (Cabrera-Rubio et al., 2012). Human milk also contains an abundance of complex oligosaccharides with prebiotic activity, stimulating the growth of beneficial bacteria such as Bifidobacteria (Zivkovic et al., 2011).

65. The intestinal microbiota plays important functional roles in a diverse range of processes including, for example, the development of immune tolerance, the nitrogen economy of the young infant, and endogenous production of vitamin K.

Renal function

66. The renal function of healthy term infants is well developed at birth and matures rapidly during the first six months (Guignard, 1982). Historically there was much concern about the safe maximum protein and electrolyte content of the diet associated with the use of unsuitable breastmilk substitutes such as whole cows’ milk and introduction of solid foods as early as the first few months of life (Fomon & Ziegler, 1999). This led to modification in the composition of infant formulae during the 1970s and 1980s (DH, 1996).

67. The protein and electrolyte content of breastmilk substitutes, including infant formula, remains greater than that of human milk which greatly increases both the oral solute load and the solute load presented to the kidney for excretion. Moreover reconstitution of commercially available powdered preparations is frequently inaccurate, further increasing energy density and renal solute load (Renfrew et al., 2003). Human milk contains 7-14 g protein /L (depending on the stage of lactation) if account is taken of the non-protein nitrogen fraction (Lonnerdal, 2003) which approximates some 25% of the total nitrogen content.

68. The amount of water required to eliminate urea generated by amino acid oxidation is further increased in formula-fed infants because the achievement of nitrogen balance for growth is dependent upon the effective partitioning of urea nitrogen between urinary excretion and salvage through the metabolic activity of the colonic microbiome. (Walser & Bodenlos, 1959; Waterlow, 1999). The low protein/nitrogen content of breastmilk and the effective demands for net lean tissue deposition together substantially reduce the water required for solute excretion.

69. The hydrolysis of urea by the microbiome is utilised in the synthesis of amino acids in meeting the needs of the infant. Both essential and non-essential amino acids are formed by the microbiome and are available to the infant, contributing to the effective “intake”. The amounts made available through these processes may be substantial. In breastfed infants their contribution may exceed 50% of the dietary intake during the early months of life, making an important contribution to the nitrogen economy of the young infant (Jackson 1994, Steinbrecher et al, 1996; Millward et al, 2000, Jackson et al 2004).

70. Salt intake in early life may programme the development of hypertension in later life but evidence is currently inconclusive (SACN, 2003). Population goals for salt intakes among infants were set by the Scientific Advisory Committee on Nutrition (SACN) in 2003 as <1 g salt per day (0-6 months) and 1g per day (6-12 months).

Neurological development

71. During the first year of life there is rapid neurological maturation accompanied by an increase in brain size and the number of synaptic connections. The brain doubles in overall size though there is considerable variation in the rate of regional growth. For example, cerebellar volume increases by 240 percent, and cerebral grey matter by 149 per cent but white matter by only 11 percent (Knickmeyer et al., 2008). An adequately balanced supply of nutrients is essential to support this ordered process.

72. Gross motor milestones key to independent feeding include "sitting up without support" and "crawling on hands and knees". In the World Health Organization (WHO) Motor Development Study, part of the WHO Multicentre Growth Study, the average ages at which children sat without support and crawled were 5.9 months and 8.3 months respectively (de Onis et al., 2006) but 95% confidence intervals for each were very wide: sitting without support, 3.8-9.2 months; crawling 5.2 – 13.5 months. This emphasises a need for responsiveness to the individual infant's developmental pace when interpreting population guidance.

73. Coordinated, synchronous development of social, speech and language, visual /fine motor and gross motor functioning is essential to the gradual achievement of independent feeding. Progress is usually measured by the achievement of "milestones" (Wijnhoven et al., 2004; Phatak & Phatak, 1991), the average ages at which particular skills become apparent. Within populations there is considerable inter-individual variation in the attainment of skills. Moreover, between population differences may arise from cultural variations in infant feeding practices, for example, in the timing of when finger foods are offered (Wright et al., 2011).

74. Certain feeding reflexes facilitate the acceptance of solid foods. The process by which infants ingest and process foods can be described using four types of age-related behaviours: suckling, sucking, munching and chewing. Whilst sucking and suckling are innate, munching and chewing appear to be learned as a result of exposure to different textured foods introduced once the infant is developmentally ready. Munching can occur at around four to seven months, with chewing typically developing from tip and groove the tongue to move food across the mouth as well as up seven months (WHO, 1998). By about ten months children can elevate the tongue and down. Mastication efficiency gradually increases through the first few years of life and is initially (at about six to eight months) greater for softer than harder foods (Le Reverend et al., 2014).

75. Half the infants in a UK cohort were reported by parents to be reaching for food and beginning to eat "finger foods" by six months of age; 20% reached out for food as early as four to five months and only 6% had not done so by eight

months. Generally infants whose development was most advanced in other fields also reached for food earlier (Wright et al., 2011). This behaviour may also be affected by cultural background and the type of food offered (Carruth *et al*, 2004; Carruth and Skinner, 2002; Hetzner *et al*, 2009; Khan *et al*, 2009).

World Health Organization Growth Standards

76. The achievement of linear and ponderal growth rates compatible with both short and long-term health is a key aim of early life nutrition. For many years the National Centre for Health Statistics (NCHS) growth reference formed the principal international descriptor of growth outcomes until a number of criticisms were raised. The infant data used to compile NCHS charts were from the Fels Institute (USA) growth study that included low birth weight infants and over-represented multiple births (two or more infants born from one pregnancy). Infant measurements were taken at relatively infrequent intervals (birth, one month, three months, nine months and one year) and the method of feeding was not specified.

77. These criticisms led in the 1990s to the planning and implementation of the WHO Multicentre Growth Reference Study (WHO MGRS) which was conducted in six countries between 1997 and 2003. Longitudinal and cross-sectional data were used to develop new standards describing normal growth between birth and five years of age (WHO MGRS, 2006a, 2006b), to replace the previous WHO/NCHS growth reference.

78. Certain criteria were applied to recruitment of infants to the WHO MGRS in order to ensure that growth before birth was not constrained and that infants were adequately fed:

    - All infants were born at term to healthy, non-smoking mothers who had been well throughout the pregnancy
    - Multiple births (two or more infants born from one pregnancy) were excluded
    - Infants were exclusively or predominantly breastfed for at least the first four months of life

79. The resulting growth standards describe the normal growth of a large international sample of healthy infants who were exclusively breastfed for around six months (the mean age at introduction of complementary foods was 5.4 months, WHO 2006), thereby establishing this feeding pattern as the norm.

80. The growth standards have been incorporated into age-based charts for length, weight, and Body Mass Index (BMI), which prescribe a growth outcome to be achieved in the pursuit of health. These charts are intended for use by parents,

doctors, and public health officials to monitor the growth of children and assess whether a child is too short, underweight, or overweight, for age (WHO MGRS, 2006a, 2006b).

81. In 2006, SACN, in collaboration with the Royal College of Paediatrics and Child Health (RCPCH), undertook a risk assessment of the new standards. SACN/RCPCH found that the WHO MGRS data after two weeks of age were comparable with measurements of early growth obtained in two UK cohorts. Differences were noted, however, between the birth weights of the MGRS and UK cohorts. These differences would have made the interpretation of weight change in the first two weeks of life problematic. Accordingly it was recommended that the UK combine national data for birth weight from the existing UK1990 dataset with WHO MGRS data from two weeks of age onwards.

82. The resulting UK/WHO charts prescribe the healthy growth pattern for all UK children aged two weeks to four years including those from ethnic minority groups, irrespective of whether they were breast or formula fed. Patterns of early life weight gain which deviate from these standards may have implications for future health (see Chapter 6).

Breastfeeding and infant health

Breastfeeding and infectious illness in the infant

83. The healthy neonate is born with an immature immune system that develops over several years (Gasparoni et al., 2003 and Remington, 2006). In this context, exclusive breastfeeding during the first half of infancy, followed by continued breastfeeding alongside the introduction of a more varied diet, provides infants and young children with passive specific immune protection and bears positively upon the development of immunological defence and antigenic tolerance (Hanson, 1998).

84. One of the difficulties encountered in describing the contribution of breastfeeding to infant health is that foods, liquids or nutrients may be given to the infant in addition to breastmilk, which may reduce the amount of breast milk consumed as well as introducing potential for contamination. Standard definitions have therefore been recommended to facilitate clear definition of breastmilk exposure in feeding studies.

85. Respiratory and gastrointestinal tract infections and acute otitis media (AOM; middle ear infection) are important causes of morbidity in infancy (Yuan et al., 2001). For example, in England in 2014/15, for every 10,000 emergency hospital

admissions in infants under 12 months, 522 were for respiratory tract infections and 173 for gastroenteritis[16]. Infants who are not breastfed are at greater risk of these infections in both resource rich and poorer settings, particularly in the first six months of life.

86. The U.S. Department of Health and Human Services Office on Women's Health has compiled evidence from systematic reviews/meta-analyses, randomised and non-randomised comparative trials, prospective cohort, and case-control studies quantifying the effects of breastfeeding on short and long term infant and maternal health outcomes in developed countries (Ip et al., 2007).

87. For AOM, pooled data from five cohort studies of good and moderate methodological quality comparing breastfeeding to not breastfeeding, showed a significant reduction in risk of AOM associated with breastfeeding (aOR[17]=0.60; 95%CI 0.46-0.78). Comparing ever breastfed with never breastfed, the pooled aOR of AOM was 0.77 (95%CI 0.64-0.91). Comparing exclusive breastfeeding for more than three or six months with never breastfeeding, the pooled odds ratio was 0.50 (95%CI 0.36-0.70).

88. Ip et al. (2007) identified one systematic review/meta-analysis by Chien and Howie (2001) that explored the relationship between breastfeeding and the development of gastrointestinal infections in children under one year of age living in developed countries. It was considered of fair methodological quality.

89. Sixteen studies from developed countries met the inclusion criteria set by Chien and Howie (2001); 12 prospective cohort studies, two retrospective cohort studies, and two case-control studies. The authors defined gastrointestinal infection as "any illness associated with vomiting, change in consistency or frequency of stools, or isolation of a known enteropathogenic bacterial or viral agent". Subjects were split into two groups for the final data analysis, 1) exclusive breastfeeding and partial/mixed feeding, and 2) no breastfeeding.

90. Of the 16 studies, five found a statistically significant increased risk of gastrointestinal infection in infants who were not breastfed. Most studies, however, had methodological weaknesses, such as not adequately controlling for potential confounding factors and not having clear definitions for infant feeding practices and infectious outcomes (see Methodology chapter).

---

[16] http://atlas.chimat.org.uk/IAS/dataviews/breastfeedingprofile

[17] An odds ratio (OR) is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared with the odds of the outcome occurring in the absence of that exposure. The OR is adjusted to address potential confounding.

91. Evidence from three studies that controlled for potential confounders suggested that breastfeeding was associated with a reduction in non-specific gastrointestinal infection during the first year of life in infants in developed countries (Fergusson et al., 1978; Eaton-Evans & Dugdale, 1987; Howie et al., 1990).

92. Ip et al. (2007) also identified a meta-analysis by Bachrach et al. (2003) comparing risk of hospitalisation for lower respiratory tract disease (LRTD) in healthy full term infants who were breastfed with those who were not. LRTD was defined to include bronchiolitis, asthma, bronchitis, pneumonia, empyema, and infections due to specific agents (for example, respiratory syncytial virus). The authors rated the methodological quality of the meta-analysis as grade A/good.

93. The authors considered evidence from primary studies published between 1981 and 2001, and identified seven cohort (five prospective and two retrospective) studies assessing the relationship between breastfeeding and hospitalisation risk secondary to respiratory disease, which met their inclusion criteria. These were pooled for meta-analysis and summary relative risk ratios reported.

94. Using a random effects model, infants exclusively breastfed for four or more months were significantly less likely to be hospitalised as a consequence of respiratory disease than those not breastfed (summary relative risk 0.28, 95% CI 0.14-0.54). This finding remained statistically significant after adjusting for potential confounders (socio-economic status and smoking). Infants not breastfed were 3.6 times more likely to be hospitalised compared with those exclusively breastfed for a minimum of four months. For every 26 infants exclusively breastfed for four months or more, one hospital episode secondary to respiratory disease could be prevented.

95. Since publication of the Ip et al. (2007) review the relationship between breastfeeding and risk of hospitalisation for diarrhoeal and respiratory infection in the first eight months of life has been investigated in 15,980 healthy, term infants in the UK Millennium Cohort Study (Quigley et al., 2007; Quigley et al., 2009). The main outcome measures were parental reports of diarrhoea (defined as ‘gastroenteritis’[18]) and lower respiratory tract infection (LRTI) (defined as ‘chest infection or pneumonia’) assessed by the reported age, and diagnosis at any hospital admissions in the first eight months after birth.

96. Information on infant feeding obtained through parental interview was categorised by type of milk received in the previous month (not breastfed, partially breastfed, or exclusively breastfed). Breastfeeding duration and the age at introduction of

[18] Case defined as: “someone who presented to the General Practitioner with loose stools or significant vomiting < 2 weeks, in the absence of a known non-infectious cause and preceded by a symptom-free period of 3 weeks”.

other types of milk and solids was stratified by one month age bands to estimate monthly risk of hospitalisation according to whether the infant had received solids in that month and the type of milk received in that month. The impact of age at introduction of solids on risk of hospitalisation in the presence of different milk feeding patterns was also investigated. Adjustment was made for a range of potential confounding factors (see Table 4.1 for details).

97. Infants who drank only breastmilk had a significantly lower risk of hospitalisation for both diarrhoea (aOR: 0.37; 95% CI: 0.18-0.78) and LRTI (aOR: 0.66; 95% CI: 0.47-0.92) compared with those not breastfed at all in the preceding month (Quigley et al., 2007).

98. Quigley et al. (2007) estimated that if all infants were exclusively breastfed, 53% of diarrhoea hospitalisations could be prevented and 31% could be prevented by partial breastfeeding. Likewise for LRTI, 27% of hospitalisations could be prevented with each month of exclusive breastfeeding, and 25% by partial breastfeeding.

99. In a similar prospective cohort study conducted in Spain (Paricio-Talayero et al., 2006), 1385 infants were followed from birth to one year of age to measure the association between not breastfeeding and hospital admission as a result of respiratory tract and gastrointestinal tract infections. Data on the incidence and duration of full breastfeeding (defined as exclusive or almost exclusive) were collected by maternal interview at discharge after delivery and at three, four and six months of age. The main outcome measure was hospital admission resulting from non-perinatal infection during the first year of life according to hospital records.

100. After adjustment for potential confounding variables, Paricio-Talayero et al. (2006) found that infants who were not breastfed were at significantly greater risk of hospitalisation for infections. When compared with infants fully breastfed for four or more months the risk of hospital admission for infection in the first year of life was five times higher (Hazard Ratio (HR) 4.91; 95% CI: 2.41-9.99) among never breastfed infants and over two times higher (HR 2.45; 95% CI: 1.28-4.66) among those fully breastfed fewer than four months. It was estimated that every additional month of full breastfeeding would prevent 30% of hospital admissions due to infections among those who had not received full breastfeeding; if the whole infant population were fully breastfed for four or more months 56% (95% CI: 30.9-69.4) of hospital admissions in infants under one year could be prevented.

101. A UK study embedded in the Southampton Women's Survey (SWS), a prospective birth cohort study, assessed the relationship between the duration of any breastfeeding (including mixed feeding; breastmilk alongside infant formula

and other food and drinks) and the prevalence of LRTI, ear infections and gastrointestinal morbidity during the first year of life (Fisk et al., 2011). One thousand seven hundred and sixty four infants born to SWS participants were followed up at six and twelve months of age by trained research nurses. At both visits, a detailed history of milk feeding was obtained along with data on whether the infant had suffered symptoms of the infectious diseases under investigation and whether a doctor had diagnosed the infant as having a chest infection, bronchitis, bronchiolitis, pneumonia or an ear infection. Data were collected at six months on the age at which solids were first regularly introduced.

102. The study found that there were graded decreases in the prevalence of respiratory and gastrointestinal symptoms over the first six months of life among infants who breastfed for longer. This dose-dependent relationship persisted after adjustment for a number of potential confounders (including maternal age, smoking in pregnancy, and age at which solids were first regularly introduced). For infants breastfed six months or more, compared with those who were never breastfed, the adjusted relative risks for general respiratory morbidity, diarrhoea and vomiting, were 0.72 (95% CI: 0.58-0.89), 0.43 (95% CI: 0.03-0.61) and 0.60 (95% CI:0.39-0.92), respectively. In the second half of infancy, the inverse relationship between breastfeeding duration and diagnosed respiratory infections and gastrointestinal morbidity remained, but was weaker. No significant dose-dependent association between breastfeeding duration and risk of diagnosed ear infections was observed in either the first or second six months of infancy.

Effects of introducing solid foods before six months of age

103. An extensive systematic review, (Kramer & Kakuma, 2002; updated in 2012) has assessed the effects of exclusive breastfeeding for six months compared with 3 – 4 months followed by mixed introduction of complementary liquids or solid foods with continued breastfeeding until at least six months of age. A number of infant and maternal health outcomes were studied. The review included two randomised controlled trials (Cohen et al., 1994; Dewey et al., 1999) and twenty one other studies conducted in both high and low resource settings (Adair et al., 1993; Ahn et al., 1980; Akeson et al., 1998; Brown, 1991; Castillo et al., 1996; Duijts et al., 2010; Duncan et al., 1993; Heinig et al., 1993; Huffman et al., 1987; Kajosaari and Saarinen, 1983; Khadivzadeh and Parsal, 2004; Khan, 1984; Kramer et al., 2001; Oddy et al., 1999; Onayade et al., 2004; Pisacane et al., 1995; Rao and Kanade, 1992; Savilahti et al., 1987; Simondon and Simondon, 1997; WHO, 1994; Frongillo et al., 1997) .

104. No significant differences were detected for any growth outcomes (length, weight, BMI) incidence of dental caries, cognitive ability, or behaviour at 6.5 years of age.

105. In one trial (Cohen et al., 1994), conducted in the low resource setting of Honduras, the exclusively breastfed group showed lower mean haemoglobin concentration (mean difference -5 g/L, 95%CI -8.5 to -1.5 g/L) and lower serum ferritin concentration (mean difference – 18.9 mcg/L, 95%CI -37.3 to -0.5 mcg/L) than the group who were mixed fed after four months.

106. Data from a cluster randomised trial in Belarus (Kramer et al, 2001) showed that infants exclusively breastfed for the first six months were at lower risk of gastrointestinal infection in the first year of life (RR 0.67, 95%CI 0.46-0.97) than those mixed fed from four months. Similar observations were made in a Nigerian (Onayade et al., 2004) prospective cohort study: infants exclusively breastfed during the first six months experienced less morbidity from gastrointestinal infection than those exclusively breastfed for 3 – 4 months and mixed fed thereafter. An Iranian prospective cohort study (Khadivzadeh and Parsal, 2004) observed that infants mixed fed after four months were at greater risk of both gastrointestinal and respiratory infection between four and six months of age than their exclusively breastfed counterparts.

107. An update to this review, assessing findings from 23 eligible studies, was published in 2012 and the authors' conclusions were unchanged (Kramer and Kakuma, 2012). In summary, exclusive breastfeeding during the first six months of life, as opposed to the first four with mixed feeding thereafter, is advantageous for infant health and does not adversely affect infant growth.

Continued breastfeeding following introduction of complementary foods

108. A recent systematic review (Sankar et al., 2015) identified eight cohort studies and two case control studies, all from low resource settings, reporting all-cause mortality associated with not breastfeeding after the age of six months. Relative risk of mortality among infants and children who were not breastfed, compared with those receiving any breastmilk, was 1.76 (95%CI 1.28-2.41) between six and twelve months, and 1.97 (95%CI 1.45-2.67) between twelve and twenty-three months of age. No studies from industrialized countries were identified.

109. An analysis of UK Millennium Cohort Study data on hospitalisation for diarrhoeal disease or lower respiratory infection before eight months of age showed that breastfed infants were at significantly lower risk than those not breastfed even after the introduction of non-milk foods (Quigley et al., 2009).

110. A meta-analysis of twelve cohort studies showed that the risk of acute otitis media in the first two year of life was significantly lower in infants breastfed for longer periods (OR 0.67, 95%CI 0.59 – 0.76). After the age of two years there was no effect (Bowatte et al., 2015).

Breastfeeding and maternal health

Maternal BMI

111. Analysis of pooled data from two Honduran randomised trials (Cohen et al., 1994; Dewey et al*.,* 1999) showed that mothers who breastfed exclusively during the first six months lost more weight postpartum than those who introduced other foods after four months (mean difference 0.42 kg, 95%CI 0.33-1.03 kg).

112. The impact of breastfeeding on British women's later BMI has been investigated by the Million Women Study, a prospective study of 740,628 women aged 50 – 64 years attending the NHS breast screening programme (Bobrow et al., 2013). Data on duration but not exclusivity of breastfeeding were collected by questionnaire. Among parous women, 70% had ever breastfed with a mean total duration of 7.7 ± 8.8 months. Post-menopausal BMI was significantly correlated with both parity (mean BMI increased progressively with number of births) and with breastfeeding. At each level of parity, mean BMI was significantly lower (*p* <00001) for women who had breastfed compared with those who had not; mean BMI decreased by 0.22kg/m^2. for every six months breastfeeding equivalent to an approximately 1% reduction in BMI in the study population, which in turn has been associated with an approximately 1% reduction in all-cause mortality (Prospective Studies Collaboration, 2009).

Breast cancer

113. A study of more than 147,000 women in 30 countries reported that women presenting with breast cancer had had fewer pregnancies than controls and were less likely to have breastfed (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). The relative risk of breast cancer decreased by 4.3% (95%CI 2.9-5.8, p<0.0001) for each additional year of breastfeeding. The authors concluded that *"the cumulative incidence of breast cancer in developed countries would be reduced by more than half, from 6·3 to 2·7 per 100 women by age 70, if women had the average number of births and lifetime duration of breastfeeding that had been prevalent in developing countries[19] until recently"*.

114. The European Code against Cancer programme (4th Edition) (ECaC) (Scoccianti et al., 2015) similarly estimated that there is a 2% reduction in breast cancer risk for every additional 5-months of breastfeeding during a mother's lifetime. ECaC also ranked (from highest to lowest) 30 developed nations by proportion of children ever breastfed; the United Kingdom was placed twenty-fifth.

[19] average of 6·5 births instead of 2·5 and if women breastfed each child for an average of 24 months instead of a lifetime mean of 8·7 months

Lactation[20]

115. Breast milk calcium content is homeostatically regulated, and maternal calcium intake does not alter breast milk calcium content (Olausson *et al*, 2012). The calcium demands of lactation are met by physiological changes including upregulation of maternal bone resorption (Olausson *et al*, 2012) so that most of the calcium in milk derives from the maternal skeleton. Maternal bone mineral density (BMD) can decline 5 to 10 percent during the two to six month time period of exclusive breastfeeding but normally returns to baseline during the six to twelve months following the introduction of solid foods (Kalkwarf, 1999; Olausson *et al*, 2012). Thus, a history of lactation does not increase risk of low BMD or osteoporosis in later life (Olausson *et al*, 2012).

116. The physiological responses described above (paragraph 115) appear to be similar in lactating adolescents. An analysis using NHANES III data compared BMD from dual-energy X-ray absorptiometry (DEXA) measures in 819 women ages 20 to 25 years (Chantry et al., 2004), and found that young women who had breastfed as adolescents had higher BMD than those who had not breastfed, even after controlling for obstetric variables.

Health service cost savings attributable to increased breastfeeding[21]

117. The estimated annual National Health Service cost of treating three common infant infections (and necrotising enterocolitis in preterm infants) exceeds £89 million. If all mothers breastfeeding exclusively at one week of infant age[22] were supported to continue until four months of infant age, a saving of £11 million annually could be expected solely as a consequence of the lower incidence of gastroenteritis, respiratory infection and acute otitis media (Renfrew et al., 2012; Pokhrel et al., 2014).

118. If the proportion of women who never breastfeed were halved, and 32% of women breastfed for between 7 – 18 months, over £21 million could be saved over the lifetime of 313,817 first time mothers through reduction in the risk of breast cancer (Pokhrel *et al*, 2014).

119. Additionally, it has been estimated that doubling the proportion of mothers breastfeeding for 7 – 18 months during a lifetime would reduce health service costs (at 2009-10 value) by at least £31 million through reduction in the incidence

[20] Based on the Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium (2011).
[21] Data on treatment costs and potential cost savings are based on 2009–2010 prices. The annual cohort in 2009 was 313,817 women.
[22] This proportion was 45% in 2005.

of maternal breast cancer and increasing both quantity and quality of life (Pokhrel et al., 2014).

Conclusions

120. On average, infants attain neurological maturity sufficient to participate in diversification of the diet through active acceptance of solid foods at around six months of age. There is, however, wide variation between individuals in the age at which fine and gross motor skills are attained as well as varying expectations between cultures.

121. The WHO growth standard describes the linear and ponderal growth pattern of infants who are fully breastfed for the first six months of life. It prescribes a pattern of growth to be attained by all infants whether or not breastfed.

122. Deviations from the pattern of growth described in the WHO standard, particularly upward crossing of weight centiles during infancy, are associated with the development of obesity in later life, but also with tall stature. Further research is required to monitor the quality of growth during infancy to distinguish between weight and length gain and accrual of lean body mass versus development of adiposity.

123. Breastfeeding has an important role in the development of the immune system through provision of passive specific and non-specific immune factors. There is strong epidemiological evidence that not breastfeeding is associated with an increased risk of hospital admission as a consequence of gastroenteritis or lower respiratory illness even in higher resource settings such as the United Kingdom.

124. The introduction of solid foods at three to four months is associated with greater risk of gastrointestinal, respiratory and ear infections than continuing to breastfeed exclusively.

125. Continued breastfeeding alongside other foods throughout the first year is associated with improved infant and maternal health. Women who breastfeed for longer are at lower risk of breast cancer. Each additional year of breastfeeding during a woman’s lifetime is associated with a four per cent reduction in her lifetime risk of breast cancer.

126. Compared with women who do not breastfeed or do not breastfeed exclusively, exclusive breastfeeding during the first six months is beneficially associated with greater postpartum weight loss, while the duration of breastfeeding is inversely associated with maternal BMI.

127. Increasing the prevalence of breastfeeding would be expected to yield significant health service cost savings through reduction in the risk of common infections in the infant and risk of breast cancer in the mother.

Chapter 5. Energy requirements

Dietary Reference Values for Energy (SACN, 2011)

128. In 2011, the Scientific Advisory Committee on Nutrition (SACN) published revised Dietary Reference Values (DRVs) for energy, which replaced the previous DRVs for energy set by the Committee on Medical Aspects of Food Policy (COMA) in 1991 (DH,1991). For dietary energy, DRVs are set at the average reference value, the Estimated Average Requirement (EAR). SACN has set new EAR values for dietary energy for all age groups, including infants aged 1 – 12 months (SACN, 2011).

Energy reference values for infants aged 1-12 months

129. Following the approach of the FAO/WHO/UNU Expert Consultation (FAO, 2004), SACN calculated the energy reference values for infants from total energy expenditure (TEE) plus energy deposited in newly synthesised tissue during growth.

130. TEE was predicted from a simple equation expressing TEE as a function of weight. This was derived from a longitudinal study (Butte, 2005) in which TEE was measured by the doubly labelled water (DLW) method in healthy, well-nourished, non-stunted infants, born at full term with adequate birth weight, and growing along the trajectory of the UK-World Health Organization (WHO) Growth Standard (SACN/Royal College of Paediatrics and Child Health [RCPCH], 2007). TEEs were calculated separately for breastfed, breast milk substitute fed, and for those infants where feeding is mixed or unknown.

131. Costs of tissue deposition (see Table 5.1) were calculated by applying data on the body composition of a population of healthy US infants to weight increments taken from the UK-WHO Growth Standards (SACN/RCPCH, 2007).

132. Table 5.2 shows the EAR for energy calculated by adding the estimated energy costs of tissue deposition (see Table 5.2) to TEEs for breastfed infants, breastmilk substitute fed infants and mixed fed infants. EARs for breastfed infants are lower than those for non-breastfed infants at all ages but particularly in the first three months of life.

Comparison between SACN energy reference values and the DRVs for energy from the 1991 COMA report 'Dietary Reference Values for Energy and Nutrients in the United Kingdom'

133. Table 5.4 shows energy reference values for infants in the SACN 2011 report compared with summary values reported by COMA in 1991 (in Table 2.6, DH,1991), with the change in the SACN report shown as a percentage. Some of the body weights at the various ages used to calculate values in the two reports vary slightly and this explains some of the difference although it is principally due to the different method of calculation.

134. The new energy reference values described in the SACN report are 9 – 13% higher at 0 – 3 months but compared with the COMA 1991 values are more than 15% lower in the second half of infancy (i.e. six to twelve months).

Observed energy intake and exclusive breastfeeding to six months of age

135. Some have challenged the view that exclusive breastfeeding to six months of age provides sufficient dietary energy and micronutrients to meet the requirements of the healthy infant born at term (Fewtrell, 2011; Fewtrell et al., 2011; Reilly and Wells, 2005; Reilly et al., 2005).

136. Reilly et al. (2005) conducted a systematic review to describe the metabolisable energy consumption of exclusively breastfed infants in the industrialised world at around the time that complementary feeding is introduced. Thirty-three eligible studies of 1041 mother-infant pairs measuring breast milk transfer at 3 – 4 months of age were identified. Weighted mean transfer was 779 (SD 40) g/d); six studies (99 pairs) reported transfer at five months of age (weighted mean transfer of 827(SD 39) g/d), and five studies (72 pairs) reported transfer at six months of age (weighted mean transfer of 894(SD 87)g/d). Using data from twenty-five studies on 77 mother-infant pairs, the weighted mean metabolisable energy content of breast milk was estimated as 2.6(SD 0.2) kJ/g, equivalent to 0.62kcal/g.

137. Using these data, the mean metabolisable energy intake of exclusively breastfed infants at six months was calculated as 2.2 – 2.4MJ/d (525-574kcal/d), which was less than the reference mean energy intake of 2.6 – 2.7MJ/d (632-649kcal/d) set by FAO/UNU/WHO (2004). The authors suggested that the energy needs of the average six month old infant would not be met by exclusive breastfeeding

138. More recent data however contradict this conclusion and show that exclusive breastfeeding provides sufficient energy for around the first six months of life.

Nielsen et al. (2011) recruited 50 healthy, relatively affluent, exclusively breastfeeding mother-infant pairs from breastfeeding support groups in the greater Glasgow area. Breast milk intake, energy intake (measured during the doubly labelled water, DLW, method), anthropometry and breastfeeding practices (frequency and duration of feeds) were measured at around 15 and 25 weeks of age. Forty-seven pairs completed the study, of whom 41 exclusively breastfed to 25 weeks of age.

139. At both time points, mean milk intakes were higher than values previously reported in the literature and reviewed by Reilly et al (2005). At 15 weeks, Nielsen et al reported mean milk intake was 923 (SD:122) g/d compared with 779 (SD:40) g/d at 3 to 4 months reported by Reilly et al. (2005) (p<0.001), and had increased significantly by 25 weeks to 999 (SD:146) g/d; p=0.003 (compared with literature values of 894 (SD:87) g/d at six months). The differences in milk intake reported in this study compared with literature values may be due to the use of different methodologies. In the Glasgow study (Nielsen et al, 2011), milk intakes were estimated using the DLW method while earlier literature values were based primarily on the test-weighing method.

140. Infant growth reflected WHO Child Growth Standards and energy intakes were adequate compared with reference values. Questionnaire and diary data on maternal perceptions of breastfeeding and infant behaviour indicated small and insignificant changes in feeding frequency between the two time points, and did not indicate that more time was spent on feeding with increasing age.

141. The study therefore confirmed that, when well supported, mothers following the current UK policy of exclusive breastfeeding for the first six months of life have high milk production which can increase over time to provide adequate energy intake and support normal infant growth

Feeding and regulation of intake

142. Even very young infants can regulate their intake to meet their needs. Five-day old breastfed infants randomly allocated to feed first from the left or right breast at a feed took significantly less milk from the second breast than the first. This suggested that intake was governed by the infant's appetite rather than the availability of breastmilk (Drewett & Woolridge, 1981).

143. Four-week old infants adjust breastmilk intake to conserve their energy intake when mothers change their pattern of breast usage. Offering one breast only or two breasts at each feed in random order over one-week periods led to changes in the volume of milk consumed and its mean fat concentration but not the net fat intake of the infant (Woolridge et al., 1990).

144. Fomon et al. (1969; 1975) fed ad libitum formula containing 67kcal /100ml or 133 kcal /100ml to infants for the first three months of life. Those receiving the higher energy formula took lower volumes of milk but consumed more energy overall and gained more weight until the age of six weeks. Thereafter the energy intake and weight gain of the two groups was similar. This suggests that energy density may influence the weight gain of non-breastfed infants in the early weeks of life but that they are able to regulate intake more effectively after six weeks of age.

145. Caregiver control and responsiveness to the infant's feeding cues may also affect intake as the infant develops socially during the early years of life. Feeding style may vary in a number of ways; for example infants may be fed to a schedule or be fed on demand; bottle-fed infants may be given fixed volumes of milk regardless of cues; parents may attempt to encourage greater consumption if their infant is considered underweight, or offer less if considered overweight.

146. The extent to which caregiver responsiveness modifies the infant's self-regulation of intake is currently unclear. There is a lack of interventional research and the majority of observational studies in this area are cross-sectional thus the direction of causality is unclear. The methodology adopted to measure caregiver responsiveness has also been inconsistent (DiSantis et al., 2011; Hurley et al., 2011).

Evidence from randomised controlled trials

Breastfed infants

147. In two randomised controlled trials (RCTs) conducted in Honduras, exclusively breastfed infants were allocated either to continue breastfeeding exclusively to six months of age or receive solid foods alongside breastfeeding from four months (Cohen et al., 1994; Dewey et al., 1999). No growth differences were observed between groups in either of the studies. In both studies breastmilk intake fell in the groups given solids but the total energy intake of the two groups was no different. This suggests that the introduction of solid foods before six months displaces, but does not increase, breastmilk energy intake.

148. More recently, an RCT in Iceland (Wells et al., 2012) recruited 119 mother-infant pairs exclusively breastfeeding[23] at four months and randomly assigned them to continue breastfeeding exclusively (EBF, n=61; completed n=50) or to receive complementary foods from four months with continued breastfeeding (CF, n=59; completed n=50). All mothers were counselled by lactation

[23]The operational definition of exclusive breastfeeding was breastfeeding with no additional liquid or solid foods other than vitamins and medications, although up to a maximum of 10 feedings of formula or water during the first six months were allowed because of practicalities of breastfeeding.

specialists. Breast milk intake was estimated using the stable isotope deuterium dose-to-the-mother method. Anthropometric outcomes were also measured and intakes of complementary foods in the complementary feeding group were assessed using three-day weighed records.

149. The exclusively breastfeeding group consumed 83 g/d (95% CI: 19, 148 g/d) more breast milk than did the complementary feeding group (P=0.012), equivalent to 53kcal/d. Infants in the complementary feeding group obtained a mean daily energy intake of 63 $\pm$ 52kcal/d from complementary foods. Estimated total energy intakes were similar (EBF: 560 $\pm$ 98 kcal/d; CF: 571 $\pm$ 97kcal/d) and there were no significant differences in anthropometric outcomes (height, weight and head circumference) and body composition between the two groups.

Non breastfed infants

150. Mehta et al. (1998) randomly allocated 165 non-breastfed infants to four diet groups: 1). commercial solid foods three to twelve months of age, 2). parental choice of solid foods three to twelve months of age, 3). commercial solid foods six to twelve months of age, 4) parental choice of solid foods six to twelve months of age. Energy intake from solid foods and from infant formula was measured at three, six, nine and twelve months. Measurements of weight, length, head circumference and body composition (dual energy x-ray absorptiometry) were also made at these intervals.

151. There were no between-group differences in total energy intake, growth or body composition measurements at any age but infants given solid foods at three months took significantly less infant formula than those introduced to solid foods from six months.

Conclusions

152. The EAR for dietary energy in infancy is based on achievement of the growth pattern of infants exclusively or predominantly breastfed for around the first six months of life. SACN’s recently revised estimates of EAR for dietary energy of infants six to twelve months old (2011) are more than 15% lower than those previously set by COMA in 1991.

153. Older estimates of breastmilk energy intake were largely obtained from cross-sectional studies prone to bias. A recent observational study using the more accurate DLW method has confirmed that breast milk production increases between four and six months to meet the energy demands of the growing infant.

154. A recent randomised trial has confirmed the findings of earlier trials: giving complementary foods to breastfed infants before six months compromises breastmilk intake without increasing total energy intake or achieving growth advantage over infants who continue to be exclusively breastfed.

155. Behavioural experiments suggest that breastfed infants regulate energy intake as early as the first week of life (Fomon *et al*, 1975). Similarly, the early introduction of solid foods (from four months) to breastfed infants results in a compensatory reduction of breast milk intake with no increase in total energy intake or change to the rate of growth (Cohen et al., 1994; Dewey et al., 1999; Wells et al., 2012)

156. Some limited evidence suggests that formula-fed and breastfed infants differ in their ability to regulate milk intake; formula fed infants may not do so until they are over six weeks of age.

157. There is no evidence that breastfeeding exclusively for the first six months of life constrains energy intake or infant growth. A succession of randomised trials has shown that giving complementary foods to breastfed infants before six months compromises breastmilk intake without increasing total energy intake or increasing weight gain and is associated with other negative health outcomes.

Chapter 6. Infant feeding, body composition and health

Rate of weight gain in infancy

158. Systematic reviews of observational studies have indicated that rapid weight gain in infancy (displayed as upward crossing of centiles) is associated with an increased risk of later obesity in childhood and adulthood (Baird et al., 2005; Monteiro and Victora, 2005; Ong & Loos, 2006; Druet et al., 2012). Weight gain in infancy also reflects growth in bone and muscle as well as fat and is associated with later tall stature (Wright et al., 2012; Cameron et al., 2003) and acquisition of lean mass (Chomtho et al., 2008; Wells et al., 2005).

159. Termed “catch-up growth”, this phenomenon is also often seen in children who are born small-for-gestational-age or with a low birth weight. Catch-up growth is beneficial in the short-term by reducing the risk of hospitalisation. It has also been associated with increased adiposity in later childhood and adulthood (Ong et al., 2000; SACN, 2011). However, other studies that have examined the association between infant growth and adult obesity related morbidity, have either found no association (Jeffery et al., 2006) or an association with small size, without catch-up in infancy (Eriksson, 2011).

Age at introduction of solid foods and risk of later overweight or obesity.

Systematic review evidence

160. Moorcroft et al. (2011) conducted a systematic review of the association between the age at which solid foods were introduced to healthy term infants (≥37 weeks gestation) and obesity in infancy and childhood. The authors identified 24 eligible studies in high resource settings, including 21 prospective cohort studies, one randomised controlled trial (RCT), one reanalysis of data from two infant formula trials and one case-control study. Meta-analysis was not possible because studies varied in duration of follow-up and in the categorisation of age at introduction of solid foods. Some studies independently analysed data from the same cohorts.

161. Overall, the review did not identify consistent associations. Findings from the eight studies that measured outcomes in *infancy* (up to twelve months of age) were mixed. Four studies observed that infants introduced to solids earlier were

heavier or showed a higher weight gain (at various time points up to and including twelve months), but no overall association between age at introduction of solid foods and weight or length measures in infancy was detected. Of the nineteen studies that collected anthropometric data in *childhood* (12 months of age to 18 years), fourteen found no association between the age at which solid foods were introduced and obesity risk. Two studies, including one prospective cohort study and a case-control study, reported on obesity in adolescence (12 to 18 years) and neither found an association.

162. It is difficult in observational research to separate the effects of duration and prevalence of breastfeeding from the age at introduction of complementary foods. Most of the cohort studies identified by Moorcroft et al. did not separate formula fed, breastfed and mixed fed infants however, Haschke et al. (2000) examined the effect of age at introduction of solids on the growth of exclusively breastfed infants from the longitudinal multi-centre Euro-Growth Study. Those infants whose only milk was breastmilk but were given solids before four months of age were longer and had lower body mass index (BMI) in the first four months of life than infants introduced to solids at four to five months or older[24]. In multiple regression analysis, the age at introduction of solids was positively correlated to weight gain and change in BMI between one and twelve months of age, and to length gain between one and 24 months of age whereas duration of breastfeeding was negatively correlated to gains in weight and in length between one and twelve or between one and twenty-four months of age.

163. Another systematic review (Pearce et al., 2013) investigated the relationship between the timing of introduction of complementary feeding and overweight or obesity in childhood. Twenty three studies were identified. Four of the studies reported that a higher BMI in childhood was associated with introducing complementary foods ≤3 months or ≤4 months. Seven of the studies considered the association with body composition but only one reported an increase in percentage body fat among seven year old children given complementary foods before 15 weeks of age.

Randomised controlled trials

164. One American RCT has reported findings from a study in which 165 healthy term infants aged less than three months were randomised to receive to solid foods from three to four months or six months[25]. All infants were formula fed at

[24] At the time of publication, the World Health Organization recommended that infants should be exclusively breastfed from birth to four to six months of age.

[25] Infants in the trial were randomised to one of four groups: to receive 1) commercially prepared solid foods from 3 to 12 months, 2) commercially prepared solid foods from 6 to 12 months, 3) parent's choice of solid foods from 3 to 12 months, or 4) parent's choice of solid foods from 6 to 12 months.

recruitment but were not excluded if they had been breastfed previously. Anthropometric measurements were made throughout the first year of life and no differences between the groups were found in weight, length or fat mass (measured by DEXA) when the infants were 12 months old. The authors concluded that early introduction of solid foods did not alter growth or body composition during the first year of life (Mehta et al., 1998).

165. Of the three RCTs that investigated early introduction of complementary foods to breastfed infants (Cohen et al., 1994; Dewey et al., 1999; Wells et al., 2012) only Dewey et al. provided growth data beyond six months of age. They reported that weight-for-age and length-for-age (National Centre for Health Statistics Reference) were "similar" at twelve months of age in the groups that received solids from four or from six months of age.

Observational data

166. Since the two systematic reviews by Moorcroft *et al* (2011) and Pearce *et al* (2013) were completed, further prospective cohort studies from developed countries have reported on age at solid food introduction and subsequent risk of overweight or obesity.

167. Abraham et al. (2012) reported the complementary feeding practices of 3462 infants aged 9 – 12 months in the Growing Up in Scotland longitudinal birth cohort study (2005-2008). Introduction of complementary foods at 4 – 5 months of age, compared with 0-3 months of age was associated with a lower risk of overweight or obesity in the fourth year of life (OR = 0.74, (95% CI 0.57 – 0.97) after adjusting for birth weight, educational attainment of respondents, and quintile of Scottish Index of Multiple Deprivation score.

168. The Global Exploration of Human Milk Study is a prospective cohort of predominantly breastfeeding mother-infant pairs recruited shortly after birth in 2007 and 2008 from three urban sites: Cincinnatti, USA, Mexico City, Mexico & Shanghai, China. Age at solid food introduction was not significantly associated with weight and length measurements at one year of age (n=285), although full results were not reported (Woo et al., 2013).

169. Durmus et al. (2012) and van Rossem et al. (2013) have reported data from a longitudinal cohort of children born in Rotterdam. The age at which solid foods were introduced was not correlated with skinfold thickness at six or twelve months of age (Durmus et al., 2012), nor was it associated with weight-for-height z-scores after one year of age (van Rossem et al., 2013). The two studies differed, however, in the categorisation of age at solid food introduction: Durmus et al. grouped infants into those introduced to solids before four months, between four and five months, or after five months of age, whereas van Rossem et al. described "very early" (before three months), "early" (between three and six

months, and "timely" (after six months) introduction. van Rossem et al. reported that infants in the "early" introduction group had a higher weight gain *before* solid foods were introduced (z=0.65, 95% CI 0.34 to 0.95) than did infants introduced to solids after six months (-0.04, 95% CI -0.05 to -0.03).

170. In the Cambridge growth study cohort, age at commencement of complementary feeding between three and seven months was inversely associated with weight and length at twelve months ($P<0.01$) after adjustment for maternal and demographic factors (Vail et al., 2015). Associations were, however, attenuated after adjustment for weight and length at three months of age (i.e. *before* introduction of solid food). Moreover rapid weight gain before three months of age predicted earlier introduction of solids ($P= 0.01$), These findings were interpreted as indicating reverse causality, i.e. more rapidly growing infants were hungrier and signalled a need for earlier introduction of solids. Wright et al. (2004), in the Gateshead Millennium Baby Study, also identified rapid weight gain before the age of six weeks as a strong independent predictor of early solid food introduction, together with lower socioeconomic status, not breastfeeding, and parental perception that their infant was hungry.

171. Grote et al. (2011) pooled and analysed data from 671 healthy, formula-fed children participating in a randomised controlled trial conducted in Belgium, Germany, Poland, Italy and Spain[26]. Infants were recruited shortly after birth and followed until they were 24 months old. At three, six and nine months of age, parents were asked about the introduction of solid foods and data were grouped as: ≤3 months, 3-4 months, 4-5 months and ≥5 months[27]. Significant differences in the pattern of growth were apparent between groups. Children introduced to complementary foods ≤3 months were lighter at birth and grew faster between three and six months of age; those introduced to complementary foods ≥5 months grew more slowly in the first three months and followed a lower weight percentile over the remainder of the study period than children introduced to solids earlier. There was no significant association between age of solid food introduction and anthropometric measurements at 24 months. Three-day food diaries suggested that solids were providing additional energy rather than replacing formula.

172. Four of these prospective cohort studies (Wright et al., 2004; Grote et al., 2011; van Rossem et al., 2013; Vail et al., 2015) suggest that greater infant size or weight gain precedes the earlier introduction of complementary foods. That is,

---

[26] The original aim of the randomised trial was to compare the growth of two groups of children fed cows' milk formula with either higher or lower protein content for the first year of life, but anthropometric measurements and information about the introduction of solids was also collected.
[27] This was reported in the study by Grote et al. (2011) as ≤13 weeks, 14-17 weeks, 18-21 weeks and ≥22 weeks and has been converted to months for consistency.

associations between early age at introduction of solid foods and later overweight or adiposity are likely to reflect reverse causation.

173. Some of the inconsistencies between observational studies may be due to differing effects on breastfed versus formula fed infants (Huh et al., 2011). The timing of solid food introduction was not associated with later obesity risk (BMI ≥95th percentile for age and gender) at three years of age among breastfed children participating in the Project Viva cohort study[28] but an association was apparent amongst the children who were formula fed as infants. Formula fed infants introduced to solid foods before four months of age were significantly more likely to be obese at three years than those who started between the ages of four and five months or at six months or later. (OR 6.3, 95% CI 2.3–16.9). This remained true even when the results were adjusted for rapid early growth. Breastfeeding mothers introduced solids later; 8% of breastfed infants but 33% of formula fed infants received solids before four months. Seventeen percent of breastfed infants started solids after six months of age compared with 9% of formula fed infants ($p<0.0001$). Several other cohort studies have also reported that breastfed infants are introduced to solid foods later than formula-fed infants (Baker et al., 2004; Scott et al., 2009).

174. Birth and baseline data from 612 healthy, term infants enrolled in the NOURISH trial[29] did not identify relationships between early introduction of solids and weight gain during the study period (Mihrshahi et al., 2011). About one third (32.5%) of infants had already started on solids by the time of the baseline assessment at mean age 4.3 months (SD: 1.0) and of these infants, 24% had been introduced to solids before four months. Although the age at solid food introduction was not related to weight gain, infants in the study who were formula fed were more likely to have been introduced to solids early (OR = 2.54, 95% CI 1.26–5.13, p=0.009) and formula feeding was associated with rapid weight gain during the study period (OR = 1.72, 95% CI 1.01–2.94, p = 0.047). Feeding on schedule, rather than on demand, was also associated with rapid weight gain (OR = 2.29, 95% CI 1.14–4.61). The NOURISH trial will follow these children until they are two years old, to permit later analyses.

175. The “Hong Kong Children of 1997” birth cohort (Lin et al., 2013) reported no clear association between the age of introduction of solid foods and BMI z-score, overweight or obesity in infancy (birth to 2 years of age), childhood (2 to 8 years of age) or puberty (8 to 14 years of age) (n=7809 at follow-up). Data on the age of introduction of solid foods were, however, collected retrospectively via postal

---

[28] “Breastfed” was defined in this study as children who were at least partly breastfed for four months or more. Obesity at three years was defined as a BMI in the 95th percentile or higher, for age and gender, using United States National Reference Data.

[29] NOURISH is an Australian randomised controlled trial evaluating an intervention designed to promote positive early feeding practices and healthy food preferences in infancy and childhood.

survey in 2008, and exposure data were missing for about half of the children whose BMI z-scores were available. This suggests a high likelihood of selection and recall bias.

Quality of the complementary feeding diet

Systematic review evidence

176. A systematic review conducted by Pearce and Langley-Evans (2013) examined the relationships between later overweight or adiposity and macronutrient intake, food type/group, or concordance with dietary guidelines in the first year of life. The review cited eight prospective and two retrospective studies conducted between 1959 and 2000.

177. Four studies examined the association between high protein intake during the complementary feeding period and BMI or percentage body fat later in childhood. Studies by Hoppe *et al* (2004) in Danish infants and Günther *et al* (2007a) in German infants found no significant association with high protein intake at six to twelve months of age, and BMI or body composition in childhood. Günther *et al* (2007b) also investigated the impact of different types of protein (total, animal, dairy, meat or cereal) and found that infants with the highest animal protein intake (as percentage total energy intake) at the age of twelve months had a higher percentage body fat, while those in the highest tertiles of total, animal and dairy protein intake had a higher BMI standard deviation score at the age of seven years (Günther et al., 2007b). Protein intake at six months was not predictive. A longitudinal observational study of infant feeding and growth involving 90 Icelandic children (Gunnarsdottir et al., 2003) found that boys in the highest quartile of protein intake at nine to twelve months of age had a significantly higher BMI at six years of age compared with boys in the lowest and the second lowest quartiles of protein intakes. There was no similar association observed in girls.

178. A further UK study identified by the review (Ong et al., 2006) found that each 420 kJ/day increment in the energy intake of mixed-fed or formula fed (but not breastfed) infants aged four months was associated with a 25% increase in the risk of overweight at five years of age.

179. Pearce & Langley-Evans (2013) also found three articles from the large Southampton Women's Survey and UK Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) birth cohorts that described associations between dietary patterns at one year of age and later body composition outcomes. These studies found that dietary patterns reflecting adherence to infant feeding guidelines at one year of age were positively associated with lean mass (but not fat mass or bone mass) at four years of age.

Randomised controlled trials

180. In the European Childhood Obesity Project, Koletzko et al. (2009) conducted a multi-centre European RCT that assigned infants to receive infant and follow-on formula of differing protein concentrations for the first year of life. At the age of two years children in the low-protein group had lower weight-for-length and BMI z-scores than those in the higher protein group (0.23, 95% CI 0.089–0.36 and 0.20, 95% CI 0.06–0.34, respectively). Furthermore, the low-protein group did not differ significantly in these outcomes from a breastfed reference group. The authors concluded that the difference in weight-for-length and BMI was likely to be due to a difference in adiposity because length at 24 months did not differ between the two groups. In a follow-up analysis of this trial, Weber et al. (2014) reported higher BMI and risk of obesity at age six in the high-protein group versus the low-protein and observational breastfed group.

Cardio-metabolic outcomes

Observational data

181. Very few studies have investigated whether age at introduction of solid foods influences either the risk of cardiovascular disease or type 2 diabetes, or has an effect on measures of risk such as hypertension, blood cholesterol concentrations and insulin resistance.

182. Wilson et al. (1998) followed up 301 children from a Dundee cohort and found that being exclusively or partially breastfed as an infant was associated with a lower systolic blood pressure at the age of seven years. No significant association between blood pressure and the age of introduction of solids was reported.

183. An analysis of pooled data from birth cohort studies conducted in Brazil, India, the Philippines and South Africa (n=9640)[30] found that the age at solid food introduction (treated as a continuous variable in linear regression models) was unrelated to blood pressure and fasting plasma glucose concentrations in young adults (Fall et al. 2011).

184. Similarly, in a birth cohort of children in Mysore, India (90% of whom were breastfed for six months or more) there was no association between the age at starting "regular" complementary foods and blood glucose concentrations or insulin resistance, either at five or 9.5 years of age (n=518) (Veena et al., 2011).

[30] Data from a Guatemalan cohort was also included in the pooled analysis, but no data were available from cohort on the age at which complementary foods were introduced.

A longer duration of breastfeeding was, however, associated with better glucose tolerance at 9.5 years but not at five years of age.

185. Studies of dietary patterns during the early years have also investigated the relationship with cardio-metabolic outcomes. Using data from the UK ALSPAC study, Brazionis et al. (2013) observed that diet during the first two years of life is associated with blood pressure at 7.5 years of age; a higher score for a “less healthy” transition diet, identified using principal components analysis, was associated with an increase in systolic and diastolic blood pressure (0.62 mm Hg (9% CI 0.00 – 1.24) and 0.55 mm Hg (95% CI 0.10 – 1.00) respectively for each one standard deviation increase in diet score). The positive association remained for diastolic (but not systolic) blood pressure after adjustment for child height, BMI and waist circumference.

186. Golley et al. (2013) analysed data from the same cohort and calculated a Complementary Feeding Utility Index score to measure adherence to complementary feeding guidelines when infants were six months of age. This incorporated breastfeeding duration; age at solid food introduction; feeding to appetite; fruit and vegetables; minimising exposure to ready-made infant foods and food high in fat, salt or sugar, in addition to other components. After adjustment for factors such as birth weight and maternal education, smoking and weight status, the index score showed a weak inverse association with diastolic blood pressure at seven years of age ($\beta = -0.24$, 95% CI -0.47, -0.01, $p = 0.043$). No association was observed with blood lipid measurements or BMI.

187. The relationship between infant feeding patterns and cardiovascular development and metabolic outcomes in childhood has been investigated as part of the Generation R Study[31] (Jaddoe *et al*, 2012), a large population-based prospective cohort study from the Netherlands designed to identify early environmental and genetic causes of normal and abnormal growth, development and health, from fetal life until young adulthood. Data on breastfeeding initiation and continuation were collected by questionnaire at the infant ages of two, six and twelve months of age, and provided information on breastfeeding status (never versus ever breastfed); breastfeeding duration (<2, 2-<4, 4-<6, and $\geq$6 months); and duration of *exclusive* breastfeeding (never breastfed, partially breastfed for at least four months, and exclusively breastfed for at least four months). Timing of introduction of solid foods was determined by the age at which a fruit or vegetable snack was given for the first time (categorised as <4 months, 4-5 months). Cardiovascular measurements were conducted at a

[31] Generation R findings published since the cut-off date of end of 2015, will be considered for inclusion following consultation. These studies include: Voortman *et al*. A priori and a posteriori dietary patterns at the age of 1 year and body composition at the age of 6 years: the Generation R Study. Eur J Epidmiol 2016;31:775-783; Voortman *et al.* Protein intake in early childhood and body composition at the age of 6 years: the Generation R Study. International Journal of Obesity 2016;40:1018 -1025.

median age of six years and included systolic and diastolic blood pressure, carotid-femoral pulse wave velocity (PWV; an index of aortic stiffness), and a number of measures of cardiovascular structures (left atrial diameter [LAD], aortic root diameter [AOD], left ventricular [LV] mass, fractional shortening [FS]) (de Jonge *et al*, 2013). Fasting blood samples were collected to measure the following metabolic outcomes: high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, triglycerides, insulin and C-peptide concentrations.Total body and regional fat mass were also measured (Gishti *et al*, 2014).

188. Based on analyses of 5003 children, de Jonge *et al* (2013) found the introduction of solid foods at 4-5 months was associated with significantly higher systolic and diastolic blood pressure (p<0.01) compared with introduction after five months of age, and was associated with smaller LAD but not with other structural measures. Age at introduction of solids was also not associated with carotid-femoral PWV.

189. Cardiovascular development differed between children who were ever breastfed and those who were never breastfed, with the latter having a higher carotid-femoral PWV, a smaller LAD, and less LV mass, at six years of age, however, a dose response association with differing duration and exclusivity of breastfeeding was not observed.

190. The authors concluded that feeding patterns in infancy may affect cardiovascular development in childhood, however, further research is required to investigate whether these findings are replicated and to help elucidate the potential underlying mechanisms linking early nutrition with cardiovascular adaptations.

191. In a further study embedded in the Generation R Study (n=3417), Gishti *et al* (2014) examined the associations between infant feeding patterns and metabolic outcomes at the median age of six years, and found that duration and exclusivity of breastfeeding were not consistently associated with metabolic outcomes, while the introduction of solid foods before four months of age was positively associated with higher blood levels of total cholesterol but not with HDL and LDL cholesterol, triglycerides and insulin levels. Shorter duration of breastfeeding (<2 months) and non-exclusive breastfeeding were associated with higher risks of childhood clustering of cardio-metabolic risk factors, however, after adjusting for confounding factors, none of the associations remained significant. The authors therefore concluded that there was a lack of consistent associations between infant feeding patterns and metabolic outcomes and that further research was required to investigate this relationship.

Conclusions

192. Rapid infant weight gain in infancy has been shown to predict later overweight, but it also predicts tall stature.

193. Observational data describing associations between the age at which complementary foods are introduced and later adiposity or obesity are inconsistent. Many studies do not separate breastfed and non-breastfed infants, who may differ in their ability to regulate intake, nor characterise exclusivity of breastfeeding and its duration. This makes it difficult to separate the direct effects of solid food intake from any indirect effect through curtailment of breastfeeding.

194. In many settings, including the United Kingdom, early introduction of solid foods is closely associated with socioeconomic status and method of milk feeding. Breastfed infants are more likely to be introduced to solid foods at later ages and their parents are more likely to follow complementary feeding guidance.

195. Several prospective studies have identified rapid early weight gain as a predictor rather than a consequence of the early introduction of solids indicating a likelihood of reverse causality in any relationship between early complementary feeding and subsequent overweight.

196. Few RCTs have examined the effect of introducing complementary foods at three to four months versus at six months. The available from such studies suggests that introduction of foods other than breastmilk or infant formula before six months of age displaces rather than augments energy available from milk. No effects on growth or body composition have been observed in the first twelve months but information about weight or BMI beyond infancy is lacking.

197. There are too few data to draw conclusions about relationships between age at introduction of complementary foods and cardio-metabolic outcomes in childhood or adult life. Two studies from the same UK cohort found weak associations between diastolic blood pressure and deviation from complementary feeding guidance but no effect of age at introduction of solids was apparent in another UK cohort or in several others from low-resource settings.

Chapter 7. Micronutrients

198. A wide range of micronutrients could have been considered, however only iron, zinc, vitamin A and vitamin D were identified as key micronutrients for which questions have been raised concerning possible deficiency or excess in infancy and therefore required consideration (http://www.emro.who.int/child-health/community/family-practices/vitamin-A-iron-zinc; SACN, 2016). With regard to zinc, extensive literature searches revealed no new evidence to suggest a cause for concern from zinc deficiency in the UK setting. Literature searches revealed no evidence of vitamin A deficiency or low intakes in infants in the UK. Vitamin A toxicity however was identified as a potential concern following the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) review of the risks of toxicity from chemicals in the infant diet. The outcome of this review is summarised in Chapter 10, Table 2. Thus, the current chapter is focussed on iron, vitamin D and vitamin A. Extensive reports on Iron and Health (2010) and Vitamin D and Health (2016) have been published by SACN and provide more detailed information on biochemistry, biomarkers of exposure and toxicity (SACN, 2010; SACN 2016).

199. Assessment of the role of dietary intake for any individual micronutrient must recognise the interaction with other micronutrients in the gut and for cellular function (for example, iron in relation to zinc and copper). Furthermore, micronutrient status in infancy may not be determined simply by current dietary intake but is also influenced by the extent to which critical reserves have been acquired in utero in relation to maternal micronutrient status and duration of pregnancy. Dietary intake is inherently variable and an assessment of usual intake is less secure for relatively short periods of assessment, especially for micronutrients which are only consumed intermittently, are naturally accumulated over prolonged periods, or where absorption from gut may be compromised as in poor states of nutrition.

Iron

200. Adequate iron status is of particular importance during development of the brain and nervous system (WHO, 2001; Georgieff, 2011). Iron deficiency in infancy and early childhood, with or without anaemia, may have long-term consequences for cognitive, motor and behavioural development (Lozoff and Georgieff, 2006).

201. Iron deficiency anaemia (IDA) affects approximately 20% of pregnant women and 25% of preschool-age children worldwide (WHO, 2001; McLean et al 2009). In Europe, the prevalence of iron deficiency in preschool-age children ranges

from 3-48% (Eussen et al., 2015), however, rates of up to 80% iron deficiency have been observed in low-resource settings (WHO, 2001, Pasricha et al., 2010). For the UK, the Diet and Nutrition Survey of Infants and Young Children (DNSIYC) reported that the proportion of children with haemoglobin concentrations and serum ferritin concentrations below which iron deficiency anaemia is indicated was 3% for those aged 5 to 11 months (Lennox *et al*, 2013).

202. DRVs for iron were set by COMA in 1991 (DH, 1991) (Table 7.1) and reviewed by SACN in 2010 (SACN, 2010). An update of the evidence for the first year of life following term birth is provided in this section.

Table 7.1 DRVs for iron in the first year of life*.

Age	**Lower reference nutrient intake (LRNI)**	**Estimated average requirement (EAR)**	**Reference nutrient intake (RNI)**
0 – 3 months	0.9 (15)	1.3 (20)	1.7 (30)
4 – 6 months	2.3 (40)	3.3 (60)	4.3 (80)
7 – 9 months	4.2 (75)	6.0 (110)	7.8 (140)
10 – 12 months	4.2 (75)	6.0 (110)	7.8 (140)

*Intakes depicted in the table are in mg/d (µmol/d)

203. Other national bodies, including the US Institute of Medicine (IOM) (2001), Australia and New Zealand governments[32] (2006) and more recently, Nordic Council of Ministers (Norden, 2014) and the European Food Safety Authority (EFSA) (2013) have also issued dietary recommendations for iron. Most countries recommend intakes equivalent to the iron content of breast milk (~0.2-.3 mg/L) (Domellof et al., 2004). Recommendations for infants from six to twelve months are in the order of ~ 8 mg/day, although higher intakes at 11 mg/day are recommended in the USA, Australia and New Zealand.

Assessment of iron status in infants and young children

204. Serum ferritin and haemoglobin concentrations are the most commonly cited markers of iron status but the thresholds chosen to indicate deficiency have been much debated (Table 7.2). Serum ferritin concentration reflects systemic ferritin depots. Low serum ferritin concentrations represent low depots but may not represent a functional deficiency of iron. Ferritin behaves as an acute phase reactant and concentrations are raised in response to acute and chronic inflammation including mild infections (Hulthen et al, 1998). Thus, acute phase markers (for example, high sensitivity CRP) are usually

[32] Australian National Health and Medical Research Council (NHMRC), Australian Government Department of Health and Ageing and the New Zealand Ministry of Health (NZ MoH).

measured alongside serum ferritin to indicate the presence of infection and allow exclusion.

205. Additional biomarkers of iron status including transferrin saturation, soluble transferrin receptor, reticulocyte haemoglobin and hepcidin concentrations are becoming more widely available but require further evaluation in infants (see SACN 2010 as well as extensive reviews by Dömellof et al., 2014; Hernell et al., 2015).

Table 7.2 Comparison of international definitions of iron deficiency and iron deficiency anaemia in infants and young children.

Indicator	**Referenced by (Country)**
Iron Deficiency	
SF <10 µg/L	NHANES (USA), NDNS (UK), Zhou et al. 2012 (Australia)
SF <12 µg/L	World Health Organisation 2004, SACN 2010 (UK)
SF <15 µg/L	Hay et al. 2004 (Norway), Copozzi et al. 2010 (Italy)
SF <12 µg/L + MCV <74 fl	Michaelsen et al. 1995 (Denmark), Gunnarsson et al. 2004 (Iceland)
Iron Deficiency Anaemia	
Hb <110 g/L + SF <12 µg/L	World Health Organisation (2004), SACN 2010 (UK)
Hb <110 g/L + SF <15 µg/L	Hay et al. 2004 (Norway)
Hb <105 g/L + SF <10 µg/L	Zhou et al. 2012 (Australia)
Hb <105 g/L + SF <12 µg/L + MCV <74 fl	Michaelsen et al. 1995 (Denmark), Gunnarsson et al. 2004 (Iceland)

SF: serum ferritin; MCV: mean corpuscular volume; Hb: haemoglobin; NHANES: National Health and Nutrition Examination Survey; NDNS: National Diet and Nutrition Survey; SACN: Scientific Advisory Committee on Nutrition.

206. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition (2014) recommends age-specific cut-offs for defining IDA from birth to 5 years (Domellof et al., 2014). During infancy, these values are Hb 135 g/L + SF 40 µg/L during the first week of life, decreasing to Hb 90 g/L + SF 40 µg/L at 2 months, Hb 105 g/L + SF 20 µg/L at 4 months and Hb 105 g/L + SF 10-12 µg/L from six to twelve months.

207. The UK Diet and Nutrition Survey of Infants and Young Children (DNSIYC) reported on the iron status of British infants 4-18 months of age in 2013. The proportions of children with both a haemoglobin concentration and a serum ferritin concentration below SACN thresholds (Table 7.2) were 3% at

5 to 11 months and 2% at 12 to 18 months. Further findings are provided in Chapter 10.

Iron status at birth

208. Fetal iron stores increase throughout gestation. At 20 and 40 weeks gestation, the fetus contains about 58 and 94µg of iron respectively per gram of lean tissue (Dallman et al, 1988). During the last trimester, the fetus accumulates about 2mg of iron daily and the mature term neonate contains 150-250mg of iron, of which almost 80% is in haemoglobin (1g of haemoglobin contains 3.47mg iron). Much of the remainder is in the reticuloendothelial and hepatic tissue iron depots.

209. Some studies have reported no significant associations between maternal and cord haemoglobin or ferritin concentrations (Kilbride et al., 1999, Hay et al., 2007), but others have observed that severe maternal iron deficiency, with and without anaemia, adversely affects fetal iron status. Infants of mothers with moderate (haemoglobin < 85 g/L) or severe (haemoglobin < 60 g/L) anaemia had significantly lower serum ferritin concentrations at birth (Singla et al., 1996). Infants born to mothers with depleted iron stores (serum ferritin < 12 µg/L) had lower cord ferritin than infants born to mothers with normal stores (Sweet et al., 2001, Jaime-Perez et al., 2005, Shao et al., 2012).

210. Additional factors including maternal obesity, smoking and pregnancy complications including gestational hypertension and growth restriction also impair intrauterine iron accretion, leading to low iron stores at birth (Hay et al., 2007; Rao and Georgieff, 2007).

211. A wide range of cord blood ferritin concentrations has been observed in newborn infants making it difficult to establish a reference range but depleted iron stores (< 76 µg/L) or severe iron deficiency (< 35 µg/L) have been associated with low mental and psychomotor developmental scores up to five years of age (Tamura et al., 2002; Siddappa et al., 2004).

212. As cord blood ferritin levels track through early infancy, those with the lowest iron stores at birth continue to have significantly lower ferritin concentrations up to two years of age (Georgieff et al., 2002; Hay et al., 2007). Studies in Spain and Jordan observed that infants born to mothers who were anaemic during their pregnancy were more likely to develop iron deficiency and IDA in the first year of life, despite no apparent effect of

maternal status on infant status at birth (Colomer et al., 1990; Kilbride et al., 1999).

213. These findings emphasize the important effect of maternal nutrition and health during pregnancy on iron stores both at birth and later in infancy.

Iron status during the first six months

214. Early clamping of the umbilical cord at delivery deprives the infant of iron. Waiting until the umbilical cord stops pulsating is associated with, on average, a 32% greater neonatal blood volume (Nelle et al., 1995) and a correspondingly increased transfer of iron (30-50 mg) to the neonate (Pisacane, 1996). McDonald et al. (2013), in an update of an earlier Cochrane review (McDonald and Middleton, 2008), concluded that delayed cord clamping resulted in improved iron stores in early infancy without increase in the risk of neonatal mortality or other neonatal morbidity outcomes. ESPGHAN has recommended that delayed cord clamping be considered for all newborns (Domellof et al., 2014) and the NICE guideline on intrapartum care for healthy women and babies (CG190, 2014) also recommends no clamping of the cord until pulsating has stopped.

215. An RCT in Sweden (Andersson et al. 2011) comparing the effects of delayed (> 3 minutes after delivery) and early (< 10 seconds after delivery) umbilical cord clamping observed a lower prevalence of iron deficiency 0.6% v 5.7%, (P=0.01) and higher serum ferritin (117 v 81 μg/L, P<0.001) at four months of age in the delayed clamping group. It is worth noting that the delayed clamping group had better neurodevelopmental outcomes at four years (Andersson et al., 2015).

216. The iron content of breast milk is low (0.2-0.4mg/L) but it is highly bioavailable (Domellöf et al., 2002). Iron deficiency in the mother has no effect on the iron content of breast milk and it is not increased by maternal iron supplementation (Zavaleta et al., 1995). Stable isotope studies have reported fractional iron absorption (incorporation of iron into erythrocytes) from breast milk of 12-21% at six months of age (Davidsson et al., 1994; Abrams et al., 1997; Domellöf et al., 2002). As mucosal uptake and transfer of iron in infants is down regulated at this age, an infant receiving 800ml/day of breast milk only absorbs about 0.05 mg/day of iron (assuming an iron content of 0.3 mg/L breastmilk and absorption efficiency of 20%). This implies that infants have no need for exogenous iron in the first six months of life and thus DRVs for infants aged 0-6 months appear to be redundant.

217. The prevalence of iron deficiency (ferritin <12µg/L) and IDA (ferritin <12µg/L and haemoglobin <105g/L) during the first six months of life in fully breastfed infants[33] was identified in six RCTs in Honduras, Ghana, Mexico and Sweden (n=404, birth weight >2500g) (Yang et al., 2009). At six months (excluding participants with elevated CRP), a prevalence of 7.9% IDA and 19.7% iron deficiency was reported. This varied greatly by country; IDA was detected in 2% in Sweden, 4% in Mexico, 5–11% in Honduras and 8–16% in Ghana. Iron deficiency was present in 6% in Sweden, 17% in Mexico, 13–25% in Honduras, and 12–37% in Ghana. Male sex, birth weight 2500–2999 g, and weight gain above the median since birth[34] were significantly associated with IDA. Iron deficiency was associated with male sex, birth weight 2500–2999g and early cord clamping. The combination of birth weight 2500–2999 g and male sex had a sensitivity of 97% for identifying IDA and 91% for iron deficiency.

218. Assuming an adequate fetal iron supply and delayed cord clamping, healthy, term, normal birth weight infants should have sufficient endogenous iron (in the form of haemoglobin iron, storage iron and functional tissue iron) to meet all their requirements for around the first six months of life (Aggett et al, 2002; Griffin and Abrams, 2001). A recent recommendation from ESPGHAN (Dömellof et al., 2014) concurs with this view.

219. All infant formulae in the European Union are fortified with iron. In its Scientific Opinion on the Essential Composition of infant and follow-on formulae, the EFSA Panel on Dietetic Products, Nutrition and Allergies has proposed a minimum content in infant formula of 0.3mg/100kcal[35]. This is because the bioavailability of iron from formula is lower than from human milk but, theoretically, infants born with adequate iron stores do not have a requirement for dietary iron in the first six months of life.

Iron status in infancy – from six to twelve months

220. After six months of age, iron stores diminish and, even with up-regulation of intestinal absorption, the amount of iron provided from breast milk is no longer sufficient to meet the increasing demands for growth and blood volume expansion. Therefore, dietary requirements for iron increase and introduction of iron-containing complementary foods from a diverse diet is recommended.

[33] Fully breastfed defined as breast milk being the only source of milk.
[34] High weight gain was defined as >4320g between birth and 6 months of age, which was the median of weight gain in the combined group of infants.

[35] http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/3760.pdf

221. Haem iron, which is the most bioavailable form of iron, is found almost entirely in food of animal origin. Non-haem iron is found in animal and plant tissues as Fe^{2+} bound to insoluble proteins, phytates, oxalates, phosphates and carbonates, and as ferritin. The richest sources of non-haem iron include cereals, vegetables, nuts, eggs, fish and meat (SACN, 2010). Iron is also added to foods as a fortificant and is available in supplemental form. The complex interactions of the prevailing diet as well as specific meal components can influence iron absorption are detailed in Chapter 5 of the SACN report on Iron and Health (2010).

222. As iron requirements at this age are driven by growth requirements, and as iron requirements largely determine iron absorption from the diet and utilisation in the body, both haem and non-haem iron are absorbed from the infant diet. To prevent low iron intakes, and to promote adequate iron status at this vulnerable life stage, dietary diversity is important for infants from six months of age.

223. There is substantial evidence that unmodified cows’ milk should not be used as a main milk drink in infants up to twelve months of age. Cows’ milk contains about 0.5-0.6mg/L of iron (DH, 1994), which is poorly absorbed because it is complexed with ligands, principally phosphate. Introduction of cows’ milk to infants aged six months has also been associated with small losses of blood from the intestinal tract (Ziegler et al., 1990).

224. Observational studies have consistently shown negative associations of unmodified cows’ milk consumption with iron status indicators throughout infancy and early childhood (Freeman et al., 1998; Male et al., 2001; Gunnarsson et al., 2004; Thorisdottir et al., 2013), while others have shown negative effects on iron stores (Michaelsen et al., 1995; Bramhagen and Axelsson, 1999; Thorsdottir et al., 2003).

225. In a large European study of twelve month old infants, the duration of cows’ milk consumption was the most consistent negative determinant of all iron status indicators; for every month of cows’ milk consumption, an average decrease of 2 g/L in haemoglobin concentrations was observed (Male et al., 2001). Several studies have reported that consumption of cows’ milk in the second six months of life (Michaelsen et al, 1995; Zlotkin, 1993) is associated with lower haemoglobin and ferritin concentrations.

226. In Iceland, dietary guidance to replace cows’ milk in the latter part of infancy (from six months) with formula resulted in significant improvements in the iron status of six to twelve month old infants (Thorisdottir et al., 2011).

Subsequently it was shown that consumption of iron-fortified products by nine to twelve month olds was associated with higher serum ferritin concentrations (Thorisdottir et al., 2013; Uijterschout et al., 2014).

Iron status and growth

227. Both body size and growth in infancy and early childhood influence iron status. Birth weight was positively associated with iron status up to one year of age (Persson et al., 1998; Sherriff et al., 1999), while weight gain in infancy was negatively associated with iron status at one year (Morton et al., 1988; Michaelsen et al., 1995; Thorsdottir et al., 2003).

228. Data from medicinal iron supplementation trials have been conflicting; a positive effect of iron supplementation on physical growth was observed (Aukett et al., 1986), but others have found none (Rosado, 1999; Ramakrishnan et al., 2009).

229. Some studies have reported an adverse effect of medicinal iron supplements on growth in iron replete infants (Idjradinata et al., 1994; Dewey et al., 2002; Majumdar et al., 2003; Lind et al., 2004).

230. Results from a double-blind RCT suggest a negative effect of medicinal iron supplements on linear growth and head circumference during infancy (Dewey et al., 2002). Full-term infants in Sweden (n=101) and Honduras (n=131) were randomly assigned at four months of age to one of three interventions groups: iron supplement (1mg/kg/day) from four to nine months; placebo four to six months and iron six to nine months; or placebo from four to nine months. All infants were exclusively or near exclusively breast fed (≤15 ml/day of foods/fluids other than breast milk and no iron fortified foods) until six months of age. Among the Swedish infants, gains in length and head circumference were significantly lower in those receiving iron supplements compared with those receiving placebo from the age of four to nine months, particularly for the six to nine month period. In Honduras, a negative effect of iron supplements on linear growth was only observed from four to six months among those with initial haemoglobin concentration of 110 g/L or above. There were no differences in head circumference among treatment groups.

231. An RCT in India (Majumdar et al., 2003) of infants aged six to twenty four months (n=150) reported that weight gain and linear growth were significantly decreased in iron replete infants (haemoglobin>110 g/L; serum ferritin>12 μg/L; n=50) supplemented with medicinal iron (2 mg/kg/day). A significant improvement in weight gain and physical growth was seen with iron

supplementation (6 mg/kg/day) of iron deficient children (haemoglobin=50‑110 g/L; serum ferritin <12 μg/L) compared with placebo.

232. Lind et al. (2004) examined the effect of medicinal iron supplementation (10 mg/day) on the growth of Indonesian iron replete infants (haemoglobin ≥113 g/L; serum ferritin ≥33 μg/L; n=154). Weight gain from age six to twelve months and mean weight at 12 months were significantly lower ($p<0.001$) in iron replete infants supplemented with iron compared with non-supplemented iron replete infants. There was no difference in linear growth between the two groups. Serum zinc levels were lower in the supplemented iron replete children (9.7 μmol/L versus 10.5 μmol/L; $p=0.04$).

233. In an RCT in Egypt (Abdelrazik et al., 2007), exclusively breastfed infants (n=248; age, four to six months) were supplemented with medicinal iron (1 mg/kg/day) or placebo for 12 months. Infants in the iron treatment group were stratified according to whether or not they were malnourished (based on anthropometric parameters) and further stratified into those with haemoglobin concentration above or below 100 g/L; all infants in the placebo group had haemoglobin values above 100 g/L. After six months of treatment, weight and length gain was significantly higher ($p<0.05$) in the iron treated group as a whole compared with the placebo group. Within the iron treated group, the increments in weight and length were significantly higher ($p<0.05$) in malnourished than nourished infants. Weight gain was greater ($p<0.01$) in malnourished infants with haemoglobin <100 g/L compared with those with haemoglobin >110 g/L; this difference was not observed in well-nourished infants. No effects were reported on head circumference.

234. A randomised trial in Brazil (Silva et al., 2008) examined the effects of different doses of medicinal iron (1 mg/kg/day, 2 mg/kg/day, or 25 mg/week) on the growth of iron replete infants (haemoglobin ≥110 g/L; age, 5‑6.9 months; n=114) supplemented for 16 weeks. The study did not include a control group. At the end of the intervention there were no statistical differences between groups in weight and length gain.

235. Iron can exert a range of acute and chronic adverse effects by competing with other transition metals of nutritional importance (for example, zinc, copper) in a number of physiological processes. It is possible that medicinal iron supplementation of iron replete children inhibits absorption of other essential nutrients required for growth, such as zinc. Although there were no differences in plasma zinc concentration between the iron treated

and placebo treated groups in the study by Dewey et al. (2002), plasma zinc concentration is not an adequate indicator of marginal zinc deficiency.

Iron status and development

236. Iron deficiency can be particularly detrimental if it occurs during critical periods of brain development, most notably the fetal or early neonatal and late infancy/early childhood periods. Depending on the timing of deficiency, different neurodevelopmental outcomes can be affected, relating to the regions of the brain developing at the time of the insult (Hensch, 2004).

237. SACN considered the extensive body of research on the relationship between IDA and cognitive, motor and behavioural development in children in its report ‘Iron and Health’ (2010). It concluded that iron deficient anaemic young children usually have poorer development than non-anaemic children but that measured and unmeasured confounding environmental variables could explain these findings.

238. SACN also concluded that, whilst RCTs of iron supplementation suggest IDA is a cause of poor motor development in children in the first three years of life (Martins et al., 2009), the long term implications of these findings in the UK are unknown. RCTs examining the effect of ID or IDA on cognitive or language development in children aged < 3 years were considered too few and follow-up too short to yield conclusions.

Adverse nutritional effects of high iron intakes

Interaction with other divalent metals

239. Interactions between divalent minerals vary according to a wide range of factors (see paragraph 7.10 of the SACN ‘Iron and Health’ report, 2010) and it is therefore difficult to determine the potential effects of increased iron intakes in early childhood on absorption and systemic use of zinc and copper and on growth. Antagonistic interactions between these minerals nevertheless have potential to negatively affect functional outcomes such as growth in infants (Sandstrom, 2001).

240. In vitro studies and studies in animal models have shown adverse effects of high levels of dietary iron on copper metabolism. Findings from the small number of human studies investigating the interactions between iron and copper also suggest that high iron intakes negatively affect serum copper

concentrations and copper metabolism (see paragraph 7.15 of the SACN ‘Iron and Health’ report, 2010, for details).

241. Domellöf et al. (2009) measured the zinc and copper absorption of breastfed infants randomly allocated to receive placebo or 1 mg /kg Fe/ d between four and nine months of age. No significant effect of iron on copper or zinc absorption was found at six or nine months of age.

Vitamin D

242. Vitamin D plays an important role in the regulation of calcium and phosphorus metabolism and is therefore important for bone health. It is synthesised in the skin upon exposure to sunlight containing sufficient ultraviolet B (UVB) radiation and this is the main source for most people. It can also be obtained from foods or dietary supplements. Dietary sources are essential when sunlight containing UVB radiation is limited (for example, during the winter months) or exposure to it is restricted (for example, due to lack of time spent outdoors or little skin exposure).

243. The Department of Health recommends that all infants from birth to one year of age who are being exclusively or partially breastfed should be given a daily supplement containing 8.5 to 10µg of vitamin D (340-400 IU/d). Infants who are fed infant formula should not be given a vitamin D supplement until they are having less than 500ml (about a pint) of infant formula a day, as infant formula is fortified with vitamin D. This is based on advice from SACN, which recommended a ‘Safe Intake[36]’ of vitamin D as data are insufficient to set RNIs for children aged under 4 years (SACN, 2016). Previously there was not a recommendation for breastfed infants, as it was assumed that maternal vitamin D supplementation during pregnancy and then breast milk would provide the infant with adequate vitamin D for the period of exclusive breastfeeding (SACN, 2016).

Dietary intakes of vitamin D

244. Data from the UK Diet and Nutrition Survey of Infants and Young Children (DNSIYC) reported average daily vitamin D intakes from all sources for ages four to six months (10.0µg); seven to nine months (8.9µg); and ten to eleven months (7.7µg) (Lennox et al., 2013). The major contributor to vitamin D intake from food for all age groups of children not receiving any breast milk was infant formula (Lennox et al., 2013). Infant formula was the largest

[36] Safe Intakes are based on a precautionary approach and reflect the insecurities of the data. They are ’judged to be a level or range of intake at which there is no risk of deficiency, and below a level where there is a risk of undesirable effects (DH, 1991).

contributor to vitamin D intake for the those aged four to six months; seven to nine months and ten to eleven months (85%, 80% and 72% respectively) followed by the food group 'commercial infant foods' (12%, 12% and 10% respectively) (Lennox et al., 2013). Vitamin D intakes for breastfed infants were not presented because the vitamin D content of breast milk is not considered to be a significant source of vitamin D or its metabolites. The reported vitamin D content of breast milk differs across studies because it varies with the type of milk measured (foremilk or hindmilk) and the time of day it is collected (SACN, 2016).

Vitamin D status

245. Serum/plasma concentration of 25-hydroxyvitamin D (25(OH)D), which is the major circulating metabolite of vitamin D, reflects the availability of vitamin D in the body from both dietary and endogenous sources. In the UK, a serum/plasma 25(OH)D concentration < 25 nmol/L is used to indicate risk of vitamin D deficiency (DH, 1998). Data from UK DNSIYC showed that the mean serum 25(OH)D for 5-11 months was 68.6 nmol/L, the lower 2.5 percentile was 12.1 nmol/L and the upper 2.5 percentile was 110.0 nmol/L. Six percent of infants had a serum 25(OH)D concentration < 25nmol/L and these were all being breastfed at the time of the stage 1 interview (Lennox et al., 2013).

Vitamin A

246. Dietary Reference Values (DRVs) for vitamin A were set by the Committee on Medical Aspects of Food and Nutrition Policy (COMA) in 1991 (DH, 1991) (Table 7.3) and dietary advice on foods and supplements containing retinol has subsequently been reviewed by SACN in its report *Review of Dietary Advice of Vitamin A* (2005).

247. SACN noted that in dietary surveys, the recording of food intake is restricted to a short continuous time period, and consequently, the habitual intake of rarely consumed foods may be over- or underestimated at an individual level (although estimates of population mean intake should be reliable). The retinol content of a few rarely consumed foods, i.e. liver and liver products, is particularly high. Consumption (or lack of consumption) of such foods during the recording period will have a substantial impact on estimates of habitual retinol intake; as a consequence, retinol intake may appear to be atypically high for some individuals and atypically low for others.

Table 7.3 Dietary Reference Values for vitamin A in the first year of life*.

Age	Lower reference nutrient intake (LRNI)	Estimated average requirement (EAR)	Reference nutrient intake (RNI)
0 – 3 months	150	250	350
4 – 6 months	150	250	350
7 – 9 months	150	250	350
10 – 12 months	150	250	350

*Intakes depicted in the table are in µg retinol equivalents/day)

248. The Government recommends that children from the age of six months to five years are given a daily supplement of vitamin A (233µg), unless they are consuming over 500ml of infant formula. This is a precautionary measure, to ensure that their requirements for these nutrients are met, at a time when it is difficult to be certain that the diet provides a reliable source.

Dietary intakes of vitamin A

249. The UK DNSIYC reported vitamin A intakes (expressed as retinol equivalents [RE]) from all sources, for four to six months, seven to nine months, and ten to eleven (Lennox et al., 2013) (Table 7.4).

Table 7.4 Intake data for vitamin A, from all sources, from the UK Diet and Nutrition Survey of Infants and Young Children (DNSIYC)*

Age	Average daily intakes from all sources	Lower 2.5 percentile intakes from all sources	Upper 2.5 percentile intakes from all sources
4 – 6 months	952	427	2052
7 – 9 months	991	370	2081
10 – 11 months	946	278	2143

*Intakes depicted in the table are in µg retinol equivalents/day

250. These data show that for infants under one year, even those with the lowest intakes of vitamin A are consuming at or around the level of the EAR, suggesting that vitamin A insufficiency is not likely to be a public health concern for this age group.

251. Infant formula was the largest contributor to vitamin A intake for infants aged four to six months, seven to nine months, and ten to eleven months (39%, 33% and 30% respectively) followed by the food group 'commercial infant foods' (23%, 25% and 23% respectively) (Lennox et al., 2013).

252. The COT assessment (http://cot.food.gov.uk/sites/default/files/cot/cotstavita.pdf) recommended a tolerable upper limit (TUL) of 200 retinol equivalents (RE)/kg bw/ day. This would approximate to a total intake of around 700 RE at birth and 2000 RE by one year. Average intakes reported in UK DNSIYC were therefore close to the TUL in the first six months and at least 2.5% were above the TUL at all ages.

Conclusions

253. Iron status at birth is an important determinant of iron status throughout infancy, particularly the first six months of life. Cord blood ferritin concentrations are correlated with ferritin concentrations until at least two years of age.

254. Factors associated with lower iron status at birth include maternal iron deficiency anaemia, low birthweight and other indicators of pregnancy risk including obesity, smoking and gestational hypertension.

255. Delaying clamping of the umbilical cord until it has stopped pulsating (about three minutes after delivery) increases neonatal blood volume, red cell mass and therefore iron status at birth.

256. During the first six months of life exclusive breastfeeding provides sufficient dietary iron for healthy, term infants of appropriate weight born with adequate iron stores.

257. From six months of age complementary foods are the principal dietary source of iron for breastfed infants.

258. There is substantial evidence that consumption of unmodified cows' milk as a main drink is associated with low iron status in infants younger than twelve months of age.

259. Evidence on the effect of medicinal iron supplements on infant growth is mixed but studies from developed countries suggest a detrimental effect on the linear growth of infants who are iron replete.

260. In relation to vitamin D, data are not available to clearly relate serum 25(OH)D concentration in the infant to current or long term non-skeletal

health. Safe Intakes[37] rather than RNIs are therefore recommended for infants and children aged up to four years. Safe Intakes are based on a precautionary approach and reflect the insecurities of the data.

261. On this basis, a ’Safe Intake’ of vitamin D is recommended in the range 8.5-10 μg/d (340-400 IU/d) for all infants from birth up to one year (whatever their mode of feeding) (SACN, 2016). The recommendation for exclusively breast fed infants is a change from previous advice. Infants who consume more than 500ml of infant formula a day do not need a vitamin D supplement as formula is already fortified.

262. The UK infant diet provides ample vitamin A, even with low uptake of supplements. For some infants who habitually consume large amounts of fortified foods such as formula milk in addition to vitamin supplements, their vitamin A intake may exceed the TUL.

[37] COMA (DH, 1991) set a *‘Safe Intake’* for some nutrients if there were insufficient reliable data to set DRVs. They are set on grounds of prudence and are *’judged to be a level or range of intake at which there is no risk of deficiency, and below a level of where there is a risk of undesirable effects’* (DH, 1991).

Chapter 8. Eating and feeding of solid foods

Determinants of food acceptance

263. A number of biological and social factors influence food acceptance and preferences during infancy and early childhood.

Biological determinants of new food acceptance

264. The sensory characteristics of foods and the sensory stimulation produced through their ingestion, including flavour, aroma and the oral perception of food texture, are key biological determinants of eating behaviour (Small and Prescott, 2005).

265. The development of acceptance of the five basic tastes (sweet, salt, bitter, sour and umami [savoury]) is not fully understood, particularly after the first six months of life (Schwartz et al., 2009). Human newborns readily accept sweet taste and have the ability to distinguish quantitative differences between different sugar solutions, demonstrating a preference for sweeter solutions and those with higher sweetening power (Desor et al., 1977; Ganchrow et al., 1983; Desor et al., 1973). At birth, reactions to salty taste are neutral ranging to rejection however, by six to twenty four months there is a well-marked preference for salty taste, which appears to decline by about 31 – 60 months (Beauchamp et al., 1986; Beauchamp et al., 1994). Data on the acceptance of bitter, sour and umami tastes are more equivocal (Schwartz et al., 2009). To help elucidate the development of taste acceptance, Schwartz et al. (2009) investigated the development of preferences for the five basic tastes at three, six and twelve months of age. They found that at each time point, sweet and salty tastes were most preferred, umami tastes produced neutral reactions, and bitter and sour tastes were the least accepted. In the same infants, Schwartz et al. (2013) examined the impact of exclusive breastfeeding on taste acceptance and found no association between the duration of exclusive breastfeeding and sweet, salty, sour and bitter taste acceptance at six or twelve months. At six months, the duration of breastfeeding was positively associated with acceptance of umami solution but by twelve months this relationship was no longer observed.

266. In a systematic review of twenty studies (the majority of which are covered in this chapter), Nehring *et al* (2015) examined the hypothesis that fetuses and infants exposed to sweet, salty, sour, bitter, umami, or specific

tastes (for example, garlic, caraway) show greater acceptance of that same taste later in life. The studies comprised 38 subgroups which were considered according to the taste under investigation and the medium in which it was presented, whether the exposure was pre- or post-natal, the child’s age at the start and end of the study, and the duration of exposure.

267. Prior exposure to bitter tastes appeared to improve acceptance of these tastes suggesting a programming effect, and there was a trend for potential programming of acceptance of specific tastes. Findings for exposure to sweet and salty tastes and later acceptance were equivocal, while there were too few studies investigating sour taste acceptance to allow firm conclusions to be drawn.

268. Heightened preference for sweet-tasting foods and beverages during infancy and childhood is observed globally and intakes of free sugars have risen consistently over recent years (PHE, 2015). It is speculated that the infant’s predisposition to reject sour and bitter tastes represents an innate response that has evolved to protect infants against ingesting toxic foods (Rozin, 1976). Conversely, the preference for sweet tastes may have evolved to attract infants and children to sources of high energy (for example, breast milk and sweet-tasting foods such as fruit) during periods of maximal growth (Ventura and Mennella, 2011).

269. Innate responses to the basic tastes can nevertheless be modified by exposure to different flavours in early life (Mennella and Trabulsi, 2012; Beauchamp and Mennella, 2009).

270. Infants experience flavours before their first exposure to solid foods. Flavours present in the mother’s diet (for example, fruit and vegetables, spices) during pregnancy, as well as those inhaled as aromas present in the environment (for example, tobacco and perfumes), may be transmitted to amniotic fluid and swallowed by the fetus (Mennella and Trabulsi, 2012), although the extent to which this occurs may vary between individuals.

271. Flavours will also be experienced by infants in breast milk, which like amniotic fluid, comprises flavours that may to some extent reflect the foods, spices and beverages consumed by the mother. As a result, the types of food eaten by women during pregnancy and lactation, and therefore the characteristic flavours of their culture, may be experienced by their infants before their first exposure to solid foods and may influence infants’ later acceptance of new foods (Mennella et al., 2001; Schaal et al., 2000). In this

way, mothers may transmit food preferences, which have a strong cultural element, to their infants.

Environmental and social factors influencing new food acceptance

272. Wide cultural and regional differences in complementary feeding practices (Mennella et al., 2006) contribute to strong preferences for regional cuisines observed in infants and children (Mennella et al., 2005).

273. The food preferences and eating habits of infants and young children are strongly shaped by their parents and caregivers' attitudes, beliefs and behaviour about food and feeding (Schwartz et al., 2011). Parents and carers act as models for eating behaviour which children learn to mirror (Savage et al., 2007). Parenting style is also associated with infant feeding habits, and can be defined by two main parental dimensions: demandingness (i.e. behavioural control over the child) and responsiveness (i.e. degree of warmth and supportiveness for the child) (Blissett, 2011). For example, a study by Moding et al. (2014) found that greater maternal responsiveness improved acceptance of new foods.

274. The feeding practices and strategies parents and carers adopt when introducing new foods impact on infants acceptance. Restricting palatable or unhealthy foods by preventing access to and/or limiting the amount consumed is a common strategy to improve children's diets or reduce the risk of unhealthy weight gain but this may be associated with poorer self-regulation of appetite and decreased intakes of fruit and vegetables. Children may also show later preference for the restricted food and increases in consumption once prohibition is lifted (Blissett, 2011).

275. The use of rewards to encourage consumption of new foods can have either deleterious or positive outcomes depending on the type of reward and the behaviour that is rewarded. For example, rewarding consumption of a new vegetable with a sweet treat tends to result in a preference for the latter and a decrease in consumption and liking for the former. Conversely, using non-food rewards tends to improve the likelihood of the new food being consumed, at least in the short-term (Birch et al., 1984).

276. Infant temperament is also associated with new food acceptance (Haycraft et al., 2011; Feldman et al., 2004; Lindberg et al., 1991; Forestell and Mennella, 2012; Moding et al., 2014). Infants who are less withdrawn, more approaching and exhibit less negative mood, display greater acceptance (as measured by increased consumption and feeding for longer periods). Infants' eating behaviour (enjoyment of food, slowness in eating, food and satiety responsiveness) also impacts on food acceptance (Mallan et al., 2014).

New food acceptance

277. During the first few months, infants tend to accept new foods with fewer exposures than at later ages. For example, they will more readily accept even quite bitter tasting formula (Mennella et al., 2011; Mennella and Beauchamp, 1998).

278. Moderate levels of food neophobia (defined as the reluctance to eat, or the avoidance of, new foods, Birch and Fisher, 1998) emerge at around 18-24 months and this is followed by a significant increase in children’s reluctance to consume new foods which peaks between two and six years of age (Cashdan, 1994; Dovey et al., 2008), after which there is a gradual decline in neophobia in most children (Cashdan, 1994; Pliner and Salvy, 2006).

279. Being a ‘picky’ or ‘fussy’ eater also influences the acceptance of new foods. In contrast to neophobia, ‘picky/fussy’ eaters are usually defined as children who consume an inadequate variety of foods through rejection of a large proportion of foods that are both familiar, and unfamiliar, to them (Dovey et al., 2008). Although parents/carers may use the term ‘pickiness’ to describe food neophobic behaviour, evidence suggests that while inter-related, ‘picky/fussy’ eating and neophobia are behaviourally distinct, with different factors predicting the severity and expression of the two constructs (Galloway et al., 2003). ‘Picky/fussy’ eating can extend further than food neophobia through children rejecting not just a particular food, but also flavours and the textures and feel of foods (Smith et al., 2005). Understanding the developmental factors that hinder the acceptance and consumption of new foods is integral to determining how to positively influence children’s food choices. The US Feeding Infants and Toddler Study (FITS) (among 4 to 24 month olds, n = 3022), included a question to caregivers on whether they considered their child a ‘picky’ eater. The prevalence of children identified as ‘picky’ eaters rose from 19% to 50% from four to 24 months, and nearly 30% of seven to 11 month olds were described by their caregivers as being ‘picky’ (Carruth et al., 2004).

280. It has been suggested that the period between four and seven months of age represents a ‘sensitive’ or ‘critical’ window for the introduction of complementary foods. It is argued that if the opportunity to introduce foods at this age is missed there may be poorer food acceptance and more food refusal both during the complementary feeding period and later in childhood (Beauchamp and Mennella, 1998; Illingworth and Lister, 1964; Mason et al., 2005; Northstone et al., 2001; Blossfeld et al., 2007; Coulthard et al., 2009; Coulthard et al., 2014). This view is, however, based on mixed evidence

which includes a limited number of case studies (Illingworth and Lister, 1964), observational studies prone to confounding, and follow-up studies (few of which followed rigorous design) of feeding difficulties experienced by children who were tube fed prior to the introduction of solid foods (Mason et al., 2005). Conclusions drawn from this weak evidence base may not be applicable to a population of healthy infants.

281. Concerns have been raised that exclusive breastfeeding during the first six months constrains the window during which new flavours and textures can be successfully introduced and accepted (Mennella and Trabulsi, 2012; Nicklaus, 2011; Fewtrell et al., 2011). The following section therefore:

a. explores the evidence for a ‘sensitive’ window for the introduction of complementary foods; and
b. investigates the key factors driving the acceptance of solid foods introduced to complement the milk diet, including the effects of repeated exposure, dietary experience, and exposure to a variety of flavours and textures, to help identify potential strategies to enhance the uptake of new foods.

282. The difficulties in conducting experimental research in this area (which include the ethical and feasibility issues associated with randomising infants to different feeding patterns and obtaining informed consent from parents), over sufficiently long periods of time and with adequate numbers of subjects, should be noted. Consequently few studies investigating the effects of major differences in feeding experience have been conducted (Mennella and Beauchamp, 2005). Those that have been carried out vary considerably in design, subject numbers, age and age range, and overall quality, making comparisons difficult.

What is the evidence supporting the view of a ‘sensitive window’ for the introduction of complementary foods?

Experimental evidence

283. Cohen et al. (1995) reported considerable resistance in the general public to recommendations to breastfeed exclusively for six months due to fears that the ‘critical’ age for learning to eat solids would be missed. To address these concerns, Cohen et al. conducted a study with the aim of determining whether the timing of introduction of solid foods to breastfed infants influenced infant appetite or acceptance of solid foods during the second half of the first year of life. In a low income, Honduran population,

mothers who had exclusively breastfed for four months were randomly assigned to continued exclusive breastfeeding to six months or to introduction of complementary foods (either with ad libitum nursing or with maintenance of baseline nursing frequency).

284. Results from this study did not support concerns that infants exclusively breastfed to six months would not accept a variety of foods as readily as those given solids at an earlier age (four months). By nine months, infants in all three study groups were eating similar amounts and types of food, consuming a similar proportion of food offered and accepting new foods equally well. Findings from a cross-sectional study in Denmark (Gondolf et al., 2011) comparing infants at nine months who were still partly breast fed with those who had completely ceased breastfeeding, also found that despite later introduction to complementary foods in the partly breastfed group, their intake of foods was similar and no delay was observed in their progression towards family foods.

Experimental evidence from studies of acceptance of protein hydrolysed formulae

285. Experimental evidence regarding the acceptance of new tastes was reported by Mennella and Beauchamp (1996), who investigated the age-related changes in the acceptance of a protein hydrolysate formula[38] (PHF). Hydrolysed protein-based formulae are described as extremely unpalatable, with a bitter and sour taste profile, unpleasant odour and aftertaste (Mennella et al., 2004). Anecdotally they are difficult to introduce to older infants with no previous exposure at an early age.

286. The study found that while infants younger than two months were able to detect the difference between PHF and their regular formulas, they drank substantial amounts of the PHF and fed to satiation. In contrast, nearly all infants aged 7-8 months old rejected the PHF ($p<0.001$), and this was apparent within the first minute of the feed. These findings therefore suggest that there may be a period during which it is possible to introduce successfully PHF which may be rejected in older infants. In a further study, Mennella and Beauchamp (1998) found a significant correlation between infants’ age and PHF acceptance ($p<0.0001$), with rejection becoming apparent between the ages of 17 – 24 weeks ($p=0.003$).

[38] Hydrolysed protein-based formulae supply protein nutrients in a ‘predigested form’. These are available on prescription for infants with diagnosed cows’ milk allergy and those infants who are unable to tolerate other intact proteins.

287. Mennella et al. (2004) found that previous exposure to PHF improved its later acceptance, with evidence of a dose effect. To help further elucidate the effects of both timing and duration of early life exposure on the acceptance of PHF, Mennella et al. (2011) randomly assigned infants to one of six groups receiving different types of formula (PHF or cows’ milk-based formula, CMF) for different durations and with varying age at initial exposure (see Table 5). Infants exposed to PHF for three months were more accepting than those infants with no exposure, but were less accepting than infants with seven months exposure. The time when flavour experience began was also significant. Infants who were first fed PHF at 3.5 months rejected it relative to the CMF to a greater extent than those infants exposed at younger ages, suggesting there may be a window for early acceptance at around 3.5 months of age.

288. In a further randomised controlled trial (RCT), Mennella and Castor (2012) investigated whether the duration of exposure to PHF affected infants’ acceptance of a food (broth) containing an exemplar of a savoury flavour during complementary feeding. They found that infants fed PHF for three or eight months, but not one month, showed greater acceptance of the savoury broth compared with the plain broth ($p<0.01$) and consumed it at a faster rate ($p<0.01$) when tested at 8.5 months of age.

289. The studies conducted by Mennella et al. have all focused on the acceptance of a specific and unpalatable bitter taste, experienced via liquid PHF. It is not known whether these findings are generalisable to the broader diversification of the diet and acceptance of other tastes, however, they provide the clearest experimental evidence in an area dominated by observational data. It is important to note that they were conducted in infants who were formula fed and it is unclear whether the findings would apply to breastfed infants who in general accept tastes more readily. Whether there is a sensitive period for the introduction of textures will be discussed later in this section.

Does repeated exposure facilitate new food acceptance?

290. It is postulated that repeated consumption of new food and flavours, when not associated with a negative gastrointestinal consequence, improves acceptance (Birch et al., 1998) and a number of studies have been conducted to more closely ascertain the number of exposures required to achieve this.

Observational evidence

291. In a longitudinal study, Sullivan and Birch (1994) examined the impact of dietary experience and type of milk feeding on the acceptance of new vegetables in infants aged between four and six months (n=36; age range 17-27 weeks, mean 22 weeks). Infants were randomised to one of four treatment groups receiving green beans or peas which were either salted or unsalted, on 10 occasions for a 10 day period.

292. Following 10 opportunities to consume the vegetable, all infants significantly increased their intake ($p < 0.001$), and acceptance increased regardless of the type of vegetable consumed. There was no clear evidence that the addition of salt increased acceptance or intake. Although there was no initial difference, after repeated exposure breastfed infants were found to have greater increases in intake of the vegetable and an overall greater level of intake, compared with formula fed infants. No dietary data were obtained from the lactating mothers and it was therefore not possible to investigate whether exposure to flavours transmitted through breastmilk influenced the breastfed infants' acceptance or intake of vegetables.

293. Birch et al. (1998) further investigated infants' initial reluctance to consume new foods and the factors that might ameliorate this response, thereby facilitating the transition to a more varied diet. In particular, they sought to establish the degree of experience with a new food required to significantly increase its intake. Whether experience with one food was sufficient to increase intake of other new foods which varied in their similarity (same, similar and different) to the target food was also examined.

294. Infants aged between 16 and 31 weeks (mean age 24 weeks) had repeated exposures to a new target food, with intake used as the measure of acceptance. A significant increase in infants' intake of the target food was observed following the exposure period ($p<0.01$), replicating findings from a previous study (Sullivan and Birch, 1994). The data showed that much of the pre-post exposure increase in intake occurred very early in the sequence of feedings; intake of the target food increased significantly ($p<0.01$) between the initial pre-test day to the first day of the exposure. Intake continued to increase during the 10 day exposure period. While intakes of the same and similar foods increased with target food exposure, intake of different foods was unchanged.

295. Findings from this study indicated that multiple exposures to the target food may not be necessary at this age (mean of 24 weeks) to produce

significant increases in intake, and suggested that for infants, relatively minimal experience (one or two exposures) with the target food, or with similar foods, can lead to significantly enhanced consumption.

296. Maier et al. (2007) investigated whether consumption of an initially disliked vegetable can be improved with repeated exposure. In the first few weeks of complementary feeding, mothers were asked to identify a vegetable purée that their infant disliked and that they normally would not offer again (mean age of infants at the start of this phase was 7.0+0.9 months). Mothers (n=49) were then asked to offer that vegetable on alternate days for 16 days, and to offer a well-liked one (carrot purée) on the other days. Nine months after the exposure period had ended (when infants were aged 15-19 months old), mothers completed a food consumption and acceptance questionnaire to ascertain whether the outcomes observed had persisted beyond the exposure period.

297. On the first day of exposure, mean intake of the initially disliked vegetable was well below that of the liked one. Over the following days, mean intake of the initially disliked vegetable increased linearly ($r = 0.99$) and significantly ($p = 0.0001$) and by the eighth exposure was similar to that of the liked vegetable. A similar pattern of results was found for mother-reported liking ratings ($r = 0.99$). Paired t-tests showed that while liking for the initially disliked vegetable was significantly lower than for the initially liked vegetable over the first six exposures, by the seventh exposure the difference was no longer significant. These effects of repeated exposure appeared to demonstrate that it is worth continuing to feed a vegetable initially disliked by infants aged about seven months; after eight exposures more than 70% of the infants in the study consumed the initially disliked vegetable. Nine months later, 63% of the infants were still eating and liking the initially disliked vegetable.

298. Acceptance of new foods (based on higher consumption and perceived enjoyment) is thus enhanced following a number of presentations. This should be viewed in the context of observational evidence showing that caregivers tend to present foods on relatively few occasions (usually less than five) before concluding that the infant will not consume the food (Carruth et al., 2004; Maier et al., 2007).

Experimental evidence

299. Building on the findings from the studies described above, more recent research has sought to investigate the effects of repeated exposure

exclusively to vegetable or fruit purées at the start of the complementary feeding period on infants' later acceptance and intake of these foods (Barends et al., 2013); test whether exposure exclusively to vegetables, compared with exposure exclusively to fruits, during the early complementary feeding period would result in a higher acceptance of vegetables; and examine whether these effects persisted at 12 and 23 months (Barends et al., 2014).

300. At the start of the intervention, infants (mean age 5.4+0.8 months) were randomly assigned to one of four treatment groups, two groups receiving exclusively vegetable purées as targets (either green beans or artichoke) and the other two groups receiving exclusively fruit purées (either apples or plums) as the target fruits for 18 days. On day 19, the vegetable groups received their first fruit purée and the fruit groups their first vegetable purée. Repeated exposure to vegetables significantly increased infants' vegetable intake, while repeated exposure to fruits had no effect on vegetable intake. Overall, fruit intake was significantly higher than vegetable intake (Barends et al., 2013).

301. In the follow-up study (Barends et al., 2014), reported daily intake of vegetables at 12 months was 38% higher in the vegetable groups than in the fruit groups (p=0.02), but by 23 months of age, was similar for both vegetable and fruit groups. The findings from these studies led the authors to conclude that initiating complementary feeding with vegetables rather than fruits may result in higher daily vegetable consumption until at least twelve months of age.

302. The consistent evidence that repeated exposure to new foods is required to improve acceptance has informed the design of studies investigating other factors influencing food acceptance during the complementary feeding period which are explored below.

How does dietary experience and exposure to a variety of flavours influence new food acceptance?

303. There is evidence that breastfed infants are more likely to accept new foods (Sullivan and Birch, 1994) and it is postulated that this may be because they experience a variety of flavours transmitted via breast milk (Maier et al., 2008; Forestell and Mennella, 2007; Mennella & Beauchamp, 1991).

304. Research in humans (Mennella and Beauchamp, 1997; Mennella and Beauchamp, 1996) and in animal models (Capretta et al., 1975; Hennessy et al., 1977; Kuo, 1967) suggests that exposure to a variety of flavours during

complementary feeding enhances the acceptance of new foods leading to consumption of a varied diet.

Experimental evidence

Effects of early exposure to flavour variety

305. Forestell and Mennella (2007) evaluated the effects of breastfeeding and dietary experiences on the acceptance of a fruit (peaches) and a green vegetable (puréed green beans) in 45 infants aged four to eight months, of whom 44% were breastfed and had never received infant formula. Infants were randomly assigned to receive either green beans alone or to receive green beans followed by peaches at the same time of day on eight consecutive days.

306. Infants who were breastfed (in most cases exclusively) for the first few months of life were more accepting of peaches when first introduced than were formula fed infants. They consumed significantly more peaches ($p<0.001$), for longer periods of time ($p<0.01$) at a faster rate ($p<0.03$) and displayed fewer negative facial responses. The authors hypothesised that this effect might be the result of their greater exposure to fruit flavours via breast milk as the mothers of the breastfed infants ate significantly more fruits during the previous week than other mothers ($p<0.04$).

307. Repeated dietary exposure to green beans, with or without peaches, led to significant increases in infants' consumption of green beans ($p<0.001$) and the rate at which they ate this food ($p<0.001$), in both breast and formula fed infants, supporting findings reported above (Sullivan and Birch, 1994; Birch et al., 1998; Maier et al., 2007).

308. Infants fed green beans and peaches together made fewer distaste facial expressions when eating green beans following the eight day exposure period, than before (no difference was observed in the number of facial displays pre- and post-test period in infants exposed only to green beans). These findings were consistent with previous research suggesting that liking for a bitter tasting vegetable (or beverage) is enhanced if it is associated with sweet tastes (Stein et al., 2003; Havermans and Jansen, 2007), but not salt.

309. To test the hypothesis that exposure to a variety of flavours at the beginning of the complementary feeding period facilitates the acceptance of new foods in formula fed infants, Gerrish and Mennella (2001) assessed acceptance of a new vegetable (puréed carrot) and meat (puréed chicken) in three groups of infants (16 infants/group) following a nine day exposure period

during which group one was fed only carrots, group two only potatoes, and group three was fed a variety of vegetables that did not include carrots.

310. Infants in the carrot and variety groups, but not those in the potato group, ate significantly more carrots following the nine day exposure period than at baseline (p=0.002 and p=0.003 respectively). Infants in the variety group also showed enhanced acceptance of chicken when compared with the carrot group.

311. The authors concluded that exposure to a variety of flavours (albeit still relatively limited at this stage) at the start of the complementary feeding period enhances the acceptance of new foods.

312. Maier et al. (2008) later examined whether breastfeeding[39] modified the effects of vegetable variety on new food acceptance early in the complementary feeding period.

313. One hundred and forty seven breast or formula fed infants (mean age at the start of the study + SEM: 5.2+0.1 months) were split into three groups. All received the same vegetable (carrot purée) as a first meal and, over the next nine days, group one received carrots every day, group two had three vegetables each given for three consecutive days, and group three had the same three vegetables but with daily changes. On the 12th and 23rd days, the infants' acceptance of two new vegetable purées, and several weeks later, meat and fish, was assessed.

314. Breastfeeding was associated with higher intakes of the four new foods introduced during the intervention period (p<0.0001), and the degree of variety also had a significant effect (p<0.0001), the high vegetable variety group (group three) showing the greatest increase in intake of new food. A significant interaction (p=0.0009) between type of milk feeding and degree of variety was noted, breastfeeding and high variety in combination being associated with the greatest intake of new foods. This effect was still present two months later at the end of the intervention period[40]. Both breastfeeding and high variety were significantly associated with higher liking scores as rated by mothers (p=0.005 and p<0.0001, respectively) and observers (p=0.008 and p<0.0001, respectively).

---

[39] Breastfeeding was defined as breastfed for >30 days and formula feeding was defined as breastfed for <15 days.

[40] Experimental design: new foods given in 3 phases (phases A, B and C). Phase A: days 0-12; phase B: days 13-23; a variable delay before phase 3 (mean ± SEM: 21.7 ± 1.8 days); phase C: 14 days.

315. The authors concluded that enhanced acceptance of new foods might be best achieved by making frequent (daily) changes in the solid foods offered as opposed to offering foods for three consecutive days in rotation.

316. The impact of advising parents to introduce a variety of single vegetables as first foods on infants' subsequent acceptance of new foods, has been investigated in a European multi-centre intervention study[41] (Fildes et al., 2015). Mothers of infants aged four to six months were randomised to either an intervention group (n=75) receiving advice to introduce five vegetables (one per day) as first foods over fifteen days, or a control group (n=71) who received country-specific standard government complementary feeding guidance. One month after the intervention, infants' consumption and liking of a new, unfamiliar, vegetable was assessed.

317. Analyses of the combined results for the three countries found no significant intervention effect but analyses by country found a significant effect in the UK sample. Both intake (p=0.003) and liking (maternal and researcher rated) of the unfamiliar vegetable (p<0.001) were increased in the UK infants but not in the Greek or Portuguese sample. The authors postulated that their findings reflect the UK tendency traditionally to offer foods other than vegetables as first foods. If so, repeated exposure to a variety of vegetables early in the complementary feeding period might beneficially affect new food acceptance.

318. Mennella et al. (2008) further explored the effects of an eight day exposure to a single food or to a variety of foods on the acceptance of fruit and vegetables in infants aged between four to nine months (n=74).

319. The first phase of this study (the fruits study) tested the hypothesis that repeated dietary experience with either one fruit (pears) or a variety of fruits (not including pears) would enhance infants' acceptance of pears without modifying their acceptance of green beans (which taste more bitter and less sweet than pears).

320. The second phase of this study (the vegetables study) explored whether providing a variety of foods within a meal as well as between the target meals (given on days one and eleven) differentially affected the acceptance of the target vegetables. Infants were split into three groups: a group fed just green beans for the eight days home exposure period; a group fed a variety of vegetables between the target meals (BM); and a group fed a

[41] Conducted in the UK, Greece and Portugal

variety of vegetables both between meals and within meals (BM-WM). The BM group received only one vegetable each day (green and orange vegetables alternated daily) while the BM-WM group were fed two vegetables each day (one green, one orange) during the eight days of home exposure.

321. After eight days of dietary exposure to pears or a variety of fruits between meals, Mennella et al. observed a significant increase in pear consumption but this enhanced acceptance was not generalisable to green beans. Repeated exposure to a variety of vegetables between meals also did not alter the acceptance of green beans, carrots or spinach. The authors concluded that the flavour of the foods experienced must relate to the target food in order for new foods to be accepted. For example, to enhance the acceptance of bitter vegetables such as green beans, infants may require more exposures and these should include foods that are bitter tasting (Stein et al., 2003).

322. Following eight days of exposure to a variety of vegetables, infants in the BM-WM vegetable variety group consumed significantly more green beans (p=0.002) as well as carrots and spinach (p=0.03).

323. These findings suggest that a number of dietary factors alter acceptance of fruit and vegetables; the flavour(s) of foods offered, whether the dietary exposure occurred between or within meals or both, and whether the target food was a fruit or vegetable. Repeated exposure to the target food was associated with improved acceptance, although this did not appear to generalise to other foods. Experience of a variety of flavours and foods also enhanced acceptance.

324. The effect of different vegetable exposure methods (variety compared with single taste) on new food acceptance has also been investigated in infants of differing age. UK infants (n=60) were introduced to solids either before the age of 5.5 months (mean age of introduction 4.50 months), or after 5.5 months (mean age of introduction 5.91 months) (Coulthard et al., 2014). Infants’ acceptance of carrot was measured at baseline prior to a nine day exposure period which commenced a week after infants had first been introduced to solid foods. During the exposure period, the two groups of infants were divided further so that half of each group received carrot every day while the other half were given a variety of vegetables. At the end of this period, infants’ acceptance of a new food, pea purée, was measured.

325. Neither age at introduction of complementary foods nor exposure type affected consumption of the baseline vegetable (carrot). Consumption of the

new vegetable (pea) after the nine day exposure period was also unaffected. There was, however, a significant interaction between age of introduction and exposure type: infants who had been introduced to complementary foods later, and who were exposed to a variety of vegetables, consumed significantly more of the new food (pea purée) than those who had only received carrots ($p<0.05$). This study suggests that offering a variety of tastes may be particularly important for parents/carers following recommendations to introduce complementary foods at around six months.

326. Hetherington et al. (2015) have also explored whether a gradual step-by-step introduction to vegetables during early complementary feeding would facilitate the transition from the exclusively milk diet and whether any exposure effect would generalise to another unfamiliar vegetable. They further examined whether effects remained apparent six and 18 months later.

327. Infants were recruited before solid foods were introduced and randomised to an intervention group (n=18) or to a control group (n=18). The intervention group received 12 daily exposures to vegetable purée added to the infants’ usual milk followed by 12 x 2 daily exposures to vegetable purée added to rice. The control group received plain milk and rice. Both groups then received 11 daily exposures to vegetable purée. At the end of this 35 day period, the intervention group consumed more of the vegetables than the control group, ate these foods more rapidly, and according to investigator ratings, liked these foods more, than the control group. The effects were specific to the exposed vegetables and there was no enhanced acceptance of the unfamiliar vegetable. No group differences were observed by six and 18 months follow up.

328. This study confirms that repeated presentation of a variety of vegetables enhances food acceptance but suggests that any effect may not persist beyond the first few months.

Observational evidence

329. A longitudinal study of 203 French infants (Lange et al., 2013) described maternal feeding practices in the first year of life and investigated influences on later acceptance of new foods. Mothers recorded each food offered from the beginning of the complementary feeding period (average age five months) to the age of 15 months and scored acceptance of each for the first four presentations.

330. Neither the duration of exclusive breastfeeding nor the age at introduction of complementary foods impacted on infants' acceptance of new foods. No differences were detected between infants introduced to complementary foods before or after six months of age (p=0.22). The majority of new foods were accepted (91%) but fruits and vegetables were the least well accepted food categories at the beginning of complementary feeding period. Earlier introduction of vegetables was associated with better acceptance of new vegetables.

331. The total number of new foods offered during the two month period after complementary feeding commenced (i.e. food variety) was significantly associated with the acceptance of new foods (p=0.02) until 15 months of age. This was most marked for the fruit (p = 0.04), vegetable (p = 0.002) and meat (p=0.02) categories.

How do the textural characteristics of food affect new food acceptance?

332. It is has been claimed that delay in the introduction of chewable, more lumpy textured foods may compromise acceptance of new textures at later ages, adversely affecting the variety of the diet (Nicklaus, 2011). The evidence supporting this hypothesis is limited however to a few observational studies.

Observational evidence

333. In a group of 12 month old infants (n=70; mean age:52.7+2 weeks), Blossfeld et al. (2007) examined infants' acceptance of cooked carrots prepared in two different textures; puréed and chopped. For all participants, carrots were a regular component of the complementary feeding diet and had been introduced between 16 and 25 weeks of age.

334. Infants consumed significantly more of the puréed carrots than the chopped carrots (p<0.0001) and mothers' ratings of the infants' enjoyment for this texture was significantly higher (p<0.01). While these findings suggested that at twelve months of age, infants have a strong preference for the puréed version of carrots, considerable individual variability was observed in the measurements. Further analysis was therefore conducted to help identify the drivers for acceptance of different textures.

335. Consumption of chopped carrots was best predicted by the infants' previous experiences with different textures. Being introduced early to complex textures (for example, mashed or lumpy foods) was positively

associated with eating chopped carrots, although the authors did not state how 'early' was defined. Likewise, infants who had a greater exposure to chopped versions of different foods were more likely to eat chopped carrots. Children with more teeth ($p<0.01$), higher Dietary Variety Scores ($p<0.05$), and whose mothers perceived them to have a varied diet ($p<0.01$) consumed significantly more chopped carrots. Food responsiveness and willingness to consume new foods were good predictors for the consumption of chopped carrots, while pickiness and fussiness were negatively associated with the intake of chopped carrots.

336. The authors concluded that the acceptance of complex textures is linked to other dietary behaviours such as dietary variety, food neophobia and pickiness. They suggested that it is important to provide infants with extensive opportunities to experience not only different flavours but also a variety of different textures.

337. Northstone et al. (2001) used data collected by self-completion questionnaire as part of the UK Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) to describe the dietary patterns of infants in the UK at six and fifteen months of age and to determine the development of feeding difficulties as perceived by the mother according to the age at which lumpy solids were introduced into the diet.

338. Infants were divided into three groups according to the age at which 'lumpy' solids were first introduced: 1) before six months of age (n=1,006); 2) between six and nine months (n=6,711); and 3) after ten months of age (n=1,643). The majority of infants had commenced complementary feeding between the ages of three and four months as was recommended at the time of the study (Department of Health and Social Security, 1988).

339. Significant differences were observed in the variety of foods eaten at six and fifteen months according to the age at which lumpy solids were introduced. Compared with infants introduced between six and nine months, infants given lumpy solids before six months ate a wider variety of family foods (although this also included a larger proportion receiving highly salted adult foods, and consuming fizzy drinks and tea by 15 months), while those infants introduced to lumpy solids after 10 months had been given fewer solids of all types by six months of age, and at 15 months were significantly less likely to be having family foods. At both six and 15 months, mothers reported more feeding difficulties (including picky eating and prolonged consumption of baby foods) in those infants subsequently introduced to lumpy

solids at 10 months or older, and these infants were more likely to show definite likes and dislikes compared with the other two groups.

340. Using parental-report postal questionnaires, these children from the ALSPAC were followed up at seven years old (Coulthard et al., 2009) to examine whether late (>10 months of age) introduction to lumpy foods and exposure to a narrower variety of family foods in the first year of life (Northstone et al., 2001) was associated with later feeding difficulties and consumption of a more restricted diet. Data from all three time points (6 months, 15 months, and 7 years) were available from 7,821 children and were grouped according to the age at which lumps were first introduced into the diet: under six months of age; between six to nine months of age; and at nine months or older.

341. At seven years of age, children introduced to lumpy solids after the age of nine months, ate less of many of the food groups, and notably all 10 categories of fruit and vegetables[42], compared with the those children introduced to lumpy foods between six and nine months ($p<0.05$-0.001). Furthermore, they had significantly more feeding problems (including not eating sufficient amounts, refusal to eat the right amount, and being picky with food), at seven years of age ($p<0.05$-0.001).

342. These observational studies report associations between delayed introduction of lumpy foods, acceptance at later ages, and the incidence of feeding problems at school age. It is nevertheless important to acknowledge their weaknesses before ascribing causation to the existence of a ‘sensitive period’. There is a high likelihood of confounding and reverse causation; for example, mothers who do not expose their infants to foods of varying flavours and textures in infancy may continue this pattern into childhood; infants with less appetite may be choosier about the foods they decide to eat, and the more challenging texture of lumpy foods may be more readily refused. The authors also acknowledge the likelihood of finding more significant results by chance as a consequence of multiple statistical testing.

[42] Peas, broad beans; sweetcorn; dark green leafy vegetables; other green vegetables; carrots; other root vegetables; tomatoes; salad; citrus fruit; other fresh fruit.

Maternal/caregiver feeding practices

Baby-led weaning

343. Proponents of “baby-led weaning” (BLW), where the infant is left to entirely self-feed from the outset, with no spoon-feeding, argue that the pace of complementary feeding can be determined by the infant’s acquisition of gross and fine motor skills (Rapley, 2011). It is speculated that this approach is less coercive and enables infants to regulate their energy intake more effectively. As yet, however, the only published evidence on this is observational.

344. A retrospective questionnaire study of 155 parents of children aged 20-78 months identified a group who had adopted BLW (n=92) and a group who had followed the traditional spoon-feeding (SF) approach (n= 63) (Townsend & Pitchford, 2012). Children’s body mass index (BMI) z-score at the time of the survey was calculated using UK 1990 and Centre for Disease Control BMI references and ranked. At mean ages of 32 ± 10 months (BLW group) and 41 ± 14 months (SF group) the BLW group had slightly lower BMI than the spoon-fed group, were slightly less likely to be overweight (14.3% versus 16%) and more likely to be underweight (4.7% versus 0). In this study, however, duration of breastfeeding also differed significantly (BLW group 24 ± 11.3 months; SF group 10 ± 9.3 months, $p < 0.0001$); moreover the retrospective study design increases the risk that the results reflect reverse causation, i.e. parents had resorted to spoon-feeding of already more demanding and heavier infants. The study also found that BLW infants had higher reported preference for starchy foods and lower preference for sweet foods.

345. Two large cross sectional observational studies have confirmed that BLW is associated with earlier exposure to family foods (Brown and Lee, 2011) but one of these also found an association with low iron containing foods (Cameron et al., 2013). The authors noted, however, that only around a third of mothers who described themselves as using BLW fully adhered to it, with most also offering some spoon-feeding.

346. A randomised trial comparing BLW to conventional feeding practice is in progress in New Zealand (the BLISS study). The primary outcome measure is BMI-for-age z-score (calculated using body weight and length). Secondary outcome measures include: energy self-regulation, iron and zinc intake and status, diet quality, parental feeding behaviour, overall acceptability, choking, and growth faltering (Daniels et al., 2015).

Conclusions

347. The existence of a "critical window" for the acceptance of solid foods between four and six months is not supported by research evidence and introduction of complementary foods after six months is not associated with later difficulty in acceptance of solid foods.

348. There is experimental evidence that repeated exposure to new foods enhances acceptance, though the number of exposures required varies depending on the age of the child and the flavour in question. Some experimental evidence suggests that offering a variety of foods helps to increase acceptance of new tastes.

349. Observational evidence suggests that breastfed infants may more readily accept new foods than formula fed infants.

350. Texture should be progressed from smooth to lumpy and more complex textures throughout the first months of complementary feeding, though there is insufficient evidence to give objective guidance on the speed of progression of solid food textures Evidence seems to be restricted to observational studies and there is at present an absence of controlled studies.

351. There is insufficient evidence at present to conclude that the BLW approach to complementary feeding achieves better infant outcomes than traditional feeding practices. This approach has not been tested in a randomised controlled trial, however, observational studies suggest that it may accelerate acceptance of a wider range of textures and flavours.

Chapter 9: Oral health

Oral health of children within the UK and the impact of poor oral health

352. Oral health is part of general health and wellbeing and contributes to the development of a healthy child. Dental caries (tooth decay) is the destruction of susceptible dental hard tissues caused by acidic by-products from the bacterial fermentation of dietary carbohydrates by oral bacteria (Marsh *et al.*, 1999). This acid causes a drop in pH levels which makes the tooth susceptible to demineralisation. Demineralisation is reversible in the early stages of the process and dental caries in enamel may remineralise. Fluoride aids this remineralisation process by acting as a catalyst for the diffusion of calcium and phosphate (Selwitz *et al.*, 2007).

353. Tooth decay in early childhood is known as Early Childhood Caries (ECC) and is defined as one or more decayed, missing or filled tooth surface (dmfs) in any primary tooth of children aged under 72 months (American Academy of Pediatric Dentistry 2008)

354. Dental caries is largely preventable however it is still the most common oral disease affecting children and young people. Poor oral health impacts on children and families wellbeing and is costly to treat. The pain and infection caused by dental decay can be extremely distressing and lead to children being absent from school and parents missing work to take their children to the dentist.

355. In 2012-13, dental caries was the most common reason for hospital admission for children aged five to nine years old. Over 60,000 children aged 0-19 years were admitted to hospital to have teeth removed under general anaesthesia in 2015/16 (Health and Social Care Information Centre, 2015).

356. Although the oral health of five year olds across the UK is improving, in 2015 almost a quarter (24.7%) of five year old children in England started school with dental caries, with on average three or four teeth affected (Public Health England, 2016). In the devolved nations, the prevalence of tooth decay at five years of age is even higher; 31% of Primary 1 children in Scotland had dental caries (NHS National Services Scotland, 2016), 40% in Northern Ireland (Health and Social Care Information Centre, 2013), and for

children in Reception in Wales (2014/15) the prevalence was 35% (Cardiff University, 2016).[43]

357. Poor oral health is associated with material deprivation with children living in deprived communities having poorer oral and general health when compared with their more affluent peers (Marmot and Bell 2011). This disparity can be seen across the UK; in the English regions, 33% of five year old children in the North West experienced decay compared with 20% in the South East of England (Public Health England 2015), and these inequalities have also been demonstrated in the devolved nations where children from poorer backgrounds experienced the most decay (Morgan et al., 2015, Scottish Dental Epidemiology Coordinating Committee, 2016, The Northern Ireland Statistics and Research Agency, 2016).

358. The first survey of the oral health of three year old children in England found that 12% had experience of dental caries and those that had dental caries had, on average, three teeth affected. The early onset of this disease suggests that infant feeding practices, such as bottle feeding and complementary feeding diets, may be associated with the development of dental caries (Public Health England 2014).

UK guidance for oral health improvement

359. Evidence based guidance for oral health improvement, including the prevention of dental caries, is covered in *Delivering Better Oral Health – an evidence based toolkit for prevention* (Public Health England, 2014). The guidance relating to dental caries prevention in infants and young children (under three year olds) reiterates infant feeding advice (see paragraph 28) and also recommends that:

- from six months of age infants should be introduced to drinking from a free-flow cup, and from age one year feeding from a bottle should be discouraged
- sugar should not be added to complementary foods or drinks
- the frequency and amount of sugary food and drinks should be reduced
- parents/carers should brush or supervise toothbrushing
- start brushing as soon as the first tooth appears (usually at about six months of age), at least twice a day with fluoride toothpaste last thing at night and on at least one other occasion
- use fluoridated toothpaste containing no less than 1,000 ppm fluoride
- use only a smear of toothpaste.

[43] Children in Reception and Primary 1 are four to five years old.

360. Similar advice is provided in NICE Public Health Guideline (PH11) which states that parents and carers should be encouraged to offer drinks in a non-valved, free-flowing cup[44] from age six to twelve months, discourage feeding from a bottle from one year onwards, provide milk and water to drink between meals, and discourage parents and carers from offering baby juices or sugary drinks at bedtime (National Institute for Health and Care Excellence, 2014).

361. Free-flow cups (or beakers) are recommended because these enable the child to learn the skill of sipping which is important in the development of the muscles used in talking (American Dental Association, 2004). In Scotland, all infants are provided with a free-flow cup as part of the *Childsmile* caries prevention program (http://www.child-smile.org.uk)

Maternal diet and infant feeding practices that may impact on tooth formation and decay experience in the first 12 months of life

362. The importance of breastfeeding in protecting against infectious illnesses in the first year of life is well established (see Chapter 4).

363. Maternal diet before and during pregnancy can affect the formation and structural integrity of both the primary and permanent dentition. Cells in the oral cavity of the fetus start to differentiate to form the primary teeth at around six weeks post conception, with tooth mineralisation beginning at around four months gestation with the formation of dentine (the foundation for the deposition of enamel) (Ligh *et al*, 2001; Jontell & Linde, 1986). The nutritional status of the mother during pregnancy can directly influence the development of enamel and dentin of the child's primary and permanent teeth during fetal growth. Exposure to teratogens during pregnancy or severe maternal nutrient deficiencies can impact on the development of the primary teeth and those permanent teeth that start to form during pregnancy (Gardiner *et al*, 2008).

364. The nutritional composition of the infant diet can also have a direct effect on tooth development pre-eruption, and both the nutritional composition and the erosive characteristics of the infant diet can affect tooth tissue post-eruption. The literature on this area has not been reviewed as part of the *'Feeding in the first year of life'* review and will instead be considered in future

[44] Cups and beakers should be free-flowing vessels. Cups that can be turned upside down and retain the liquid using a non-drip (spill) valves should not be used.

risk assessments of the evidence covering young children (aged 12-60 months) and the health of women of reproductive age.

365. The oral microbiome of infants is influenced by mode of delivery; infants delivered vaginally are exposed to different microorganisms than those delivered by C-section and this may affect colonisation patterns in the oral cavity (Holgerson *et al*, 2011). This microbial colonisation initiates maturation of the infant’s immune system and alterations to the microbiota may result in illness or increased risk of infection particularly in infancy. Mode of feeding (breastfeeding versus infant formula feeding) has also been found to influence the infant oral microbiome and this may have implications for child health and long term human health (Holgerson *et al.*, 2013).

366. Teeth begin to erupt into the oral environment at around six months of age and it would be normal for infants to have both their upper central and lateral incisors erupted before twelve months (American Dental Association, 2005). As dental caries takes a finite time to develop once the teeth have erupted, any feeding practices that increase the risk of dental caries are likely only to show effects (in terms of dental caries) after the age of twelve months (Selwitz *et al.*, 2007).

367. Dental decay is caused by multi-factorial and complex interactions between cariogenic bacteria in the mouth and dietary carbohydrates that produce acids which demineralise the teeth. The evidence relating to infant feeding and dental decay is inconsistent. Factors that have been explored include: the carbohydrate content of breast milk or infant formula; factors which determine the length of contact between breast milk or infant formula and the erupted dentition (that is, frequency of feeding, and feeding practices which result in pooling of breast milk or infant formula around the teeth surfaces); and, age of colonisation and levels of cariogenic bacteria (for example, Streptococcus mutans) in an infant’s mouth. The growth and adhesion of cariogenic bacteria, particularly oral Streptococci, are inhibited by breast-specific Lactobacilli and substances including human casein and secretory IgA in breast milk which are not found in infant formula (Danielsson *et al.*, 2009, Holgerson *et al.*, 2013).

368. The risk of dental caries is also dependent on the presence of teeth and rises with increasing number of teeth. The primary teeth most at risk of early childhood caries (eight upper and lower central and lateral incisors) start to erupt at six months and are fully erupted by 12 months of age. The most vulnerable primary teeth (four upper and lower first molars) erupt between 13

and 19 months, and the remainder are erupted by 33 months (Tham *et al*. 2015). The '*Feeding in the first year of life'* review is focused on infant feeding practices up to the age of twelve months however, the risks and effects of infant feeding up to one year on the dentition are often observed in children older than 12 months of age. With diversification of the infant diet to include foods and drinks other than breast milk or infant formula, so risk changes depending on the free sugar content of the complementary foods (and drinks) and how frequently such foods are consumed.

369. Potential confounding factors need to be taken into account when considering the impact of infant and young child feeding practices on risk of dental caries. For example, formula fed infants may be more likely to be given sugar sweetened beverages in a bottle than infants who are being breastfed, while some parents/carers are more likely to follow advice on toothbrushing than others.

Breastfeeding practices and dental caries

370. In a recent systematic review, Tham *et al* (2015) identified 63 papers reporting on associations between breastfeeding and ECC and used this evidence to assess the potential impact of breastfeeding when undertaken up to 12 months of age and for over 12 months of age, on risk of dental caries.

371. The quality of the studies within this systematic review was assessed using the Newcastle-Ottawa Scale (NOS) Assessment which examined the following categories (which are independently scored a maximum of two per category): representativeness, selection of non-exposed cohort, ascertainment of exposure, outcome of interest not present at start, comparability, assessment of outcome, adequate follow-up time and adequate follow-up of cohorts.

372. Tham *et al* (2015) identified two cross sectional studies that compared breastfeeding 'ever' within the first 12 months versus breastfeeding 'never' within the first 12 months. These studies were categorised as 'satisfactory' in quality using the NOS Assessment for Cohort Studies. Both studies demonstrated a protective effect of breastfeeding when considering dental caries compared with other feeding (Du *et al.*, 2000, Qadri *et al.*, 2012), however, they were undertaken in China and Syria respectively and the generalisability to UK populations may therefore be limited. Furthermore, data were collected retrospectively; children's feeding practices were assessed by questionnaire when the children were between two to four years

and two to five years of age, which might result in recall bias and weakened confidence in the strength of the findings.

373. Tham *et al* also identified a prospective cohort study which was designed to assess the association between infant breastfeeding and caries experience in US children (Hong *et al.*, 2014). The study had a sample of 509 subjects recruited from birth for whom the following data were collected: two clinical dental exams (at five and nine years old), and demographic and breastfeeding information collected via questionnaires. This study was rated as good using the NOS assessment although Tham *et al* (2015) reported that the study did not have an adequate follow up of their cohort.

374. The study observed that at five years of age, 16% of children who were breastfed less than six months had caries (mean decayed filled surface=0.55) while only 9% of children who were breastfed for at least six months had caries. From five to nine years old, caries incidence was 32% and 31%, respectively, for children breastfed less than six months and for at least six months. In multivariable regression analyses, shorter breastfeeding duration was positively associated with caries experience at five years old (p=0.005), both before and after controlling for other important factors (Hong *et al.*, 2014). Tham *et al* (2015) concluded that infants who were breastfed in the first 12 months of life had fewer dental caries compared with formula fed babies.

375. Tham *et al* (2015) also reviewed the evidence relating to dental caries and breastfeeding on demand (Prakash *et al,* 2012 in urban India) and breastfeeding *ad libitum* during the night (Azevedo *et al.*, 2005 in Brazil and Parera *et al*, 2014 in Sri Lanka). Three further studies examined the impact of sleeping with the breast in the mouth (Sayegh *et al.*, 2005, Johansson *et al.*, 2010, Retnakumari *et al.*, 2012). These studies were undertaken in a deprived community in Jordan, Boston (USA) and Kerela (India) and respectively and therefore the generalisability to UK-based populations may therefore be limited. Using the NOS, the studies were assessed and scored for quality and were found to be of variable quality, with only one study controlling for confounders (Sayegh *et al*. 2005).

376. Although frequently analysed as separate behaviours, nocturnal breastfeeding, breastfeeding on demand, and an infant falling asleep with the breast in the mouth, are often interrelated. The studies considered by Tham *et*

al found significant correlations between these breastfeeding practices and an increased prevalence of dental caries.

377. Tham *et al* (2015) included studies where children were breastfed beyond 12 months. When infants are no longer exclusively breast or formula fed, confounding factors, such as the consumption of potentially cariogenic drinks and foods and toothbrushing practices, need to be taken into account when investigating the impact of infant feeding practices on caries development. Tham *et al* noted that the studies by Sayegh *et al.*, 2005, Johansson *et al.*, 2010 and Retnakumari *et al.*, 2012 did not control for possible confounders such as the introduction of complementary foods and toothbrushing with a fluoride toothpaste.

378. A single prospective cohort study of Brazilian children by Feldens *et al* (2010) (*n*=500 at baseline) investigated the relationship between feeding practices in the first year of life (assessed at six and twelve months of age) and the occurrence of severe ECC at four years of age (*n*=340; any sign of smooth-surface caries is indicative of severe early childhood caries (American Academy of Pediatric Dentistry, 2008)). This study was rated 'good' for its quality using the NOS scale overall, however, was scored as poor with regards to comparability of the cohorts within the study (Tham et al. 2015).

379. A higher adjusted risk of severe ECC was observed when dietary practices at twelve months included: breastfeeding over seven times daily (RR = 1.97; 95% CI = 1.45-2.68) compared with once or twice daily or not breastfed; intake of foods with a high density of sugar[45] (RR = 1.43; 95% CI = 1.08-1.89); bottle use for liquids other than milk (RR = 1.41; 95% CI = 1.08-1.86); and more than eight meals and snacks consumed daily (RR = 1.42; 95% CI = 1.02-1.97). The authors acknowledged that the increased risk of severe ECC might be related to other cariogenic factors within the child's diet. They also noted that maternal schooling for more than eight years was associated with decreased dental caries in the child (Feldens *et al.*, 2010).

380. Tham et al (2015) concluded that with regard to associations between breastfeeding over 12 months and dental caries 'further research with careful control of pertinent confounding factors is needed to elucidate this issue and better inform infant feeding guidelines'.

[45] High density of sugar was regarded as a proportion > 50% of simple carbohydrates in 100g of food (for example, candies, soft drink, sugar and honey).

Breastfeeding versus bottle feeding and dental caries

381. Avila *et al* (2015) systematically reviewed the evidence relating to the association between feeding practice (breastfeeding versus bottle feeding) and dental caries in childhood (Avila *et al.*, 2015). The content of bottles was not reported in all of the studies within this review and there was therefore a lack of clarity regarding the impact of bottle versus breastfeeding because bottle fed children may have been consuming infant formula alone and/or other drinks from a bottle. Where the single studies within this review provided information on the contents of the bottle, this is stated in the following paragraphs.

382. Seven studies were identified and their quality was rated using the NOS Assessment (five cross-sectional studies, one case-control and one cohort study). All studies assessed feeding practices by questionnaire. In the three cross-sectional studies (Al-Dashti *et al.*, 1995, Du *et al.*, 2000, Qadri *et al.*, 2012) and the cohort study (Majorana *et al.*, 2014), breastfed children were less frequently affected by dental decay than bottle fed children.

383. Al-Dashti *et al* (1995) undertook a cross sectional study in Kuwait to identify the prevalence and extent of caries in early childhood. Mothers of pre-school children were interviewed and their children (aged 18 to 48 months) received a dental examination. Of the 227 children examined, 107 (47 per cent) were caries free, and 41 (18%) had five or more decayed, missing or filled teeth. Caries in at least two incisors was seen in 19% of the children. The study found that breastfed children were less affected by caries than bottle fed children ($p<0.05$). Those who were breastfed and mixed-fed (bottle and breast) were less affected by caries than those children who were bottle fed only ($p<0.05$), and breastfed children were less affected by caries than bottle fed and mixed fed children ($p<0.01$).

384. This study blinded researchers to mother's responses about feeding practices when the clinical examination was performed thus reducing the risk of bias. Whether clinical examiners had been calibrated was however, not recorded thereby reducing confidence in the reliability and reproducibility of the acquired data. Avila *et al* (2015) rated the quality of this study as moderate due to poor representativeness and comparability and the failure to adjust for confounding variables. Again, as this study utilised retrospective data collection related to dietary practices, recall bias might have been introduced and therefore caution is required when interpreting the results.

Although the study recorded "breastfeeding" versus "bottle feeding" it did not provided detail on the duration of these.

385. Du *et al* (2000) randomly selected a convenience sample of children aged 24 to 47 months (n=426, mean age = 40 months) attending six kindergartens in Hanchuan City, China and established their decay status by oral examination. Questionnaires were completed by their mothers to establish the child's infant feeding and duration of breastfeeding from birth. This study did not ascertain if there were any additions to infant formula or use of sweet drinks or other drinks in bottles. The study found that children who were fully bottle-fed (n=34, 8%) had a statistically significant higher prevalence of rampant caries[46] (p<0.01) and incisor caries (p<0.05) compared with children who had been either fully or partly breastfed (n=392, 92%).

386. The systematic review by Avila *et al* (2015) assessed Du *et al's* study as having a high risk of bias because confounding variables were not adjusted for and the representativeness of the sample was undermined. Furthermore, the study did not ascertain what additions were made to the bottle. An understanding of the use of sweet drinks in bottles would have enhanced ability to determine whether disease levels were affected by bottle feeding with the use of infant formula alone or if children who were wholly bottle-fed had additives to or sweet drinks in the bottle which influenced caries development.

387. The final cross sectional study assessed by Avila *et al* (2015) was Qadri *et al* (2012) which included 400 children aged three to five years old randomly selected from 20 kindergartens in Syria. Avila *et al* (2015) could not include this study in the meta-analysis as the data could not be extracted. They also rated the study to be at a high risk of bias as the authors did not adjust for any confounding variables and did not demonstrate calibration of examiners which may lead to unreliable results. The study was noted for having a representative sample.

388. The feeding practices were assessed by questionnaires. Breastfed children were found to be less likely to have ECC (OR: 0.27; 95%CI: 0.18–0.41; p<0.001) and had fewer decayed, missing or filled teeth (OR: 0.61; 95%

[46] sudden onset of widespread caries that affects most of the teeth and penetrates quickly to the dental pulp

CI: 0.39–0.97; p=0.038). A higher number of teeth were affected by ECC in bottle fed children (p=0.036) (Qadri *et al.*, 2012).

389. Avila *et al* (2015) included the Italian cohort study by Majorana *et al*. (2014) in the systematic review and assessed this study to have a high risk of bias related to representativeness and ascertainment for feeding habits. The study recruited 2395 toddlers aged 24–30 months and data on feeding practices, dietary habits, maternal smoking, socio-economic status and fluoride supplementation were collected from mothers via questionnaire at birth, six, nine and twelve months. A clinical exam was undertaken when the child was aged 24–30 months using the International Caries Detection and Assessment System (ICDAS). The study found significantly lower caries severity and prevalence in toddlers who were exclusively breastfed when compared with those who were mixed fed. Avila *et al* (2015) stated that in this study there was a lack of definition/diagnosis of caries and caries free children which reduced the overall quality rating of this study.

Drinking vessel used and caries development

390. There is a paucity of research in this area; only one systematic review was identified (but this was not published in English). A single retrospective study by Behrendt *et al* (2001) identified 186 children between the ages of one to six years with ECC. The most favoured drinks offered in bill-shaped vessels were fruit juices (68%), sweetened teas (23%) and unsweetened teas (26%) while lemonades and cola-drinks were given to the children less often (7.5%) (Behrendt *et al.*, 2001). The authors suggested that the prevailing outcome was that the types of drinks consumed (i.e. those with added sugar) coupled with the drinking vessel (bill-shaped) were the contributing factors for these children developing ECC.

391. The authors stated that the bill-shaped cups were similar to baby bottles with teats and were used between meals and during the night. They did not state whether the vessel was free-flowing, however the fact children were using these cups whilst sleeping would suggest the cup had a valve and operated like a baby bottle. It is difficult to draw conclusions from this study as the use of sweetened beverages and the use of fluoride toothpaste were not controlled for.

Alignment of teeth and facial growth

392. Malocclusion describes the alignment of teeth which are considered not to be in a normal position in relation to adjacent teeth (i.e. the teeth are not correctly aligned) (Nelson, 2014); the term covers a range of disorders relating to development which stem from a variety of causes.

393. Malocclusion has been suggested to vary between breast and bottle fed children. The biological plausibility is that children who are breastfed have more facial muscle activity compared with bottle-fed children and this promotes craniofacial growth and jaw bone development. The growth of the face is affected by the infant's use of their facial muscles during feeding and suckling.

394. Peres *et al.* (2015) undertook a systematic review and meta-analysis of 48 studies looking at the association between breastfeeding and facial growth and the development of malocclusion. Of the 48 studies, 13 were considered of high quality, 20 of medium quality and 15 of low quality. The meta-analysis included data for 27,023 children.

395. Meta-analysis comparing those children who were 'ever breastfed' with those 'never breast fed' found that participants ever exposed to any type of breastfeeding were less likely to develop malocclusions than those 'never breastfed' (Peres *et al.*, 2015). Those who were breastfed were less likely to develop anterior open bites and the quality of the studies did not influence the effect size. The effect on posterior cross bites was not significant.

396. When considering children who were exclusively breastfed, they had a lower risk of nonspecific malocclusions compared with those who were not exclusively breastfed. This difference was not apparent for gaps between the upper and lower front teeth (anterior open bite) or a reversal of the normal relationship between the upper and lower back teeth (posterior cross-bite). Children who were breastfed for longer were less likely to have malocclusions than those breastfed for shorter periods. The authors concluded that breastfeeding decreased the risk of malocclusions (Peres *et al.,* 2015), however, the lifetime effects of breastfeeding reducing malocclusions in the permanent dentition were not included in this review. There are no conclusions linking historic breastfeeding with orthodontic treatment need in the permanent dentition.

Conclusions

397. Current evidence suggests that breastfeeding up to twelve months of age is associated with a decreased risk of dental caries. Exclusive breastfeeding is the physiological norm for around the first six months of an infant’s life and has general and oral health benefits for the infant.

398. The consideration of children breastfed beyond twelve months was not within the remit of the evidence review. However, conclusions drawn within the Tham *et al* (2015) systematic review suggest that an increased risk of dental caries once the primary teeth erupt may occur and have association with factors such as breast feeding *ad libitum* nocturnal feeding and sleeping with the breast in the mouth. However, the authors acknowledged that the quality of most of these studies was judged as low and with the exception of a single study in Brazil confounders such as complementary feeding with cariogenic foods/drinks, or inadequate oral hygiene practices (for example, not brushing with a fluoride toothpaste) were not controlled for. Further research is required with careful control for confounding factors to inform infant feeding guidelines.

399. The data presented in this review reflects the evidence considered by one systematic review which found that ‘ever breastfed’ children were less likely to develop a malocclusion in the primary dentition compared with ‘never breastfed’ children.

Chapter 10. UK infant feeding practice

The Infant Feeding Survey

400. The Infant Feeding Survey (IFS), a national survey of infant feeding practices, was conducted every five years from 1975 to 2010. The survey provided national estimates of the incidence, prevalence, and duration of breastfeeding (including exclusive breastfeeding) and other feeding practices adopted by mothers in the first eight to ten months after their infant was born. In the more recent surveys these estimates were provided separately for England, Wales, Scotland and Northern Ireland, as well as for the UK as a whole.

401. The design of the study, questions and sampling procedure changed little since inception. This enabled the surveys to capture overall trends in infant feeding practices since 1975 and to adjust these for demographic change, notably the trend towards increasing maternal age at delivery.

402. The 2010 survey was based on an initial representative sample of mothers who were selected from all births registered between August and October 2010 in the UK. Three stages of data collection were conducted, with Stage 1 being carried out when infants were around four to ten weeks old, Stage 2 when they were around four to six months old, and Stage 3 when they were around eight to ten months old. A total of 10,768 mothers completed and returned all three questionnaires.

403. Full details of the methodology employed in and findings from the IFS 2010 can be found at http://www.ic.nhs.uk/catalogue/PUB08694; a summary of the key findings pertinent to this review is given below.

404. The findings of the 2005 IFS were reviewed by SACN in 2008. Fourteen recommendations for policy and practice were made and six recommendations for the conduct of future surveys.

Key findings on incidence, prevalence and duration of exclusive breastfeeding

405. IFS used the term "incidence" to denote the proportion of infants put to the breast, even if only once. This figure included those given expressed breastmilk. "Prevalence" denoted the proportion of infants still receiving any breastmilk at subsequent sampling stages, whether or not they were receiving other milks and liquids as well.

406. From 2005 IFS distinguished between exclusive and any breastfeeding. The prevalence of "exclusive breastfeeding" was defined as the proportion of infants who were receiving only breastmilk and had never been given other milks, liquids or solids.

407. Between 1990 and 2010 there was a 31% increase in the incidence of breastfeeding across the United Kingdom. Proportionate increases were greatest in Scotland (48% increase) and Northern Ireland (78% increase) (Table 10.1). The mother's age at birth of the infant and her age on completion of full-time education remained strong predictors of breastfeeding in the 2010 survey. Table 10.2 shows a standardised incidence for each five yearly sample adjusted for the secular change in these demographic characteristics.

408. The highest incidence of breastfeeding was observed among mothers aged 30 or over (87%), those from minority ethnic groups (97% for "Chinese or other", 96% for "Black or Black British" and 95% for "Asian or Asian British" ethnic groups), those who left education aged over 18 (91%), those in managerial and professional occupations (90%) and those living in the least deprived areas (89%).

409. Table 10.3 shows changes between 1995 and 2010 in the prevalence of breastfeeding between birth and 9-months of age. In 2010, across the UK as a whole, the prevalence of breastfeeding fell from 81% at birth to 55% at six weeks. At six months, 34% of mothers were still breastfeeding. It is apparent that the most rapid decline in breastfeeding prevalence occurs in the first two weeks of the infant's life; by six weeks of infant age 32% of mothers who initiated breastfeeding had stopped.

410. The proportion of mothers initiating breastfeeding who stopped by six weeks of age changed very little between 1990 and 2010 and was between 33-39% (Table 10.3). The reasons mothers stop breastfeeding in the early weeks have been consistently described in IFS since 1980. Table 10.4 shows data for 2005 and 2010; the principal reasons were difficulties with attachment at the breast, breast or nipple pain, and a perception that breastmilk was insufficient or the infant was hungry. The five yearly Infant Feeding Surveys also showed consistently that mothers who stopped in the early weeks would have preferred to continue had they felt able to do so. Table 10.5 shows data for 2010.

411. Table 10.6 shows the prevalence of exclusive breastfeeding in 2005 and 2010. By one week of infant age fewer than half of all mothers (46%) were exclusively breastfeeding, while this had fallen to around a quarter (23%) by six weeks. By six months, prevalence of exclusive breastfeeding

had decreased to only one percent. This percentage is very low compared with other high income countries. Thus, very few mothers followed the UK recommendation that infants should be exclusively breastfed until around the age of six months.

412. Table 10.7 shows that formula or other liquids rather than solids principally accounted for early (prior to 4-months of age) loss of exclusive breastfeeding. Only after 17-weeks did introduction of solids account for more than 2% of cases.

413. The proportion of UK women who continue to breastfeed after six months of infant age is very low compared with international statistics (McAndrew *et* al, 2012[47]) (see Table 10.3). In 2010, only 1 in 3 UK women were breastfeeding at all at six months of infant age, and only 1 in 4 at nine months of infant age. This is substantially lower than the rates observed in other high-income countries where prevalence of 55%-71% is observed at six months.

Use of milk other than breast milk

414. Almost three-quarters of mothers (73%) had given milk other than breast milk by the age of six weeks and 88% had done so by six months. Mothers from managerial and professional occupations and older mothers were likely to introduce other milks later (Table 10.8).

415. At Stage 2 of the 2010 Survey (when infants were four to six months of age), most mothers who had given their infant milk other than breast milk in the last seven days were mainly giving infant formula (88%). Use of follow-on milk or liquid cows' milk was low at this stage (nine and one percent respectively). By Stage 3 of the survey (when infants were eight to ten months of age), mothers were more likely to be using follow-on formula (57%) as their infant's main source of milk other than breast milk, rather than infant formula (35%).

416. Most mothers followed the recommendation not to give follow-on formula before the age of six months. Mothers from routine and manual occupations and those who had never worked were more likely to say they had given their infant follow-on formula at an earlier age (18% and 27% respectively at four months).

[47] The Lancet Breastfeeding Series *(*2016) published since the cut-off date of end of 2015, will be included following consultation

417. By eight to ten months of age 42% had given their infant liquid cows’ milk. Twenty-nine percent had mixed it with food while 24% had used it as an occasional drink. Only four percent of mothers had introduced liquid cows’ milk as their infant’s main milk (Table 10.9).

Liquids other than milk

418. Twenty seven per cent of mothers were giving drinks in addition to breast milk or formula by four weeks of infant age. This had risen to 55 per cent by four months and 81 per cent by six months. “Drinks” could have included water, fruit juice, squash or herbal liquids but these were not differentiated in the Survey.

419. The commonest reasons for giving drinks at Stage 1 (four to ten weeks of age) were to help with constipation (48%) or to help colic / wind / indigestion (42%). By Stages 2 and 3 (when infants were four to six months and eight to ten months respectively), the main reason for giving drinks was because the infant was thirsty (56% at Stage 2 and 86% at Stage 3).

420. At all ages up to six months fewer mothers gave drinks than in 2005. This was most evident at four months, when the proportion fell from 64% in 2005 to 55% in 2010.

421. Mothers who breastfed initially were less likely to give additional drinks before six months than those who formula fed from birth (78% compared with 92%).

422. Mothers aged under 20 were more likely than those aged 35 or over to give their infant drinks at an early age (64% and 24% respectively at six weeks old). Those from routine and manual occupation groups or who had never worked were more likely than mothers from managerial and professional groups to give drinks at an early age (48%, 44% and 25% respectively at six weeks old).

Use of cups and beakers

423. On average in 2010 mothers introduced cups and beakers a little earlier than in 2005. By six months 54% of all mothers had introduced a cup or beaker compared with 48% in 2005.

Age at introduction of complementary feeding

424. Successive five yearly Infant Feeding Surveys have documented a trend towards later introduction of solids in keeping with changes in national feeding recommendations. In 2003, the UK health departments

recommended that solid foods should be introduced when infants are around six months old. Table 10.10 shows that in 2005, 51% of mothers had introduced solid foods by four months, but by 2010, this figure had fallen to 30%. Nevertheless, 75% of mothers in 2010 introduced solids before their infant was five months old.

425. Younger mothers and those from lower socio-economic groups tended to introduce solid foods at earlier ages. Fifty-seven percent of mothers aged under 20 years and 38% of mothers in the routine and manual category or those who had never worked introduced solids by the time their infant was four months old.

426. Table 10.11 indicates mothers' reasons for introducing solid foods at various ages. The most commonly cited reason for introducing solids before four months was an unsatisfied infant (64% of mothers). Mothers who introduced solids after five months were more likely to cite written information, advice from a health professional or the infant's acquisition of motor skills as their reason.

Types of complementary foods introduced

427. Baby rice was the most common type of solid food first given to infants (57%). The majority of mothers said the food they first gave to their infant was mashed or pureed (94%), while only a small proportion gave finger food (4%).

428. When infants were four to six months old, mothers were most likely to have given them fruit or vegetables on the previous day (46%), ready-made baby foods (38%), baby rice (31%) or homemade foods (28%).

429. Table 10.12 shows the foods most frequently given when infants were eight to ten months old. Fruit and vegetables, "fresh food", breakfast cereals, cheese, yoghurt and fromage frais were the most popular items. Chicken was the most frequently offered meat. Red meats (beef, pork or lamb) were given less frequently, 46% or more of mothers offering them less than weekly or never.

Types of complementary foods avoided

430. Nearly half of mothers reported that they had consumed peanuts or peanut products during pregnancy (49%) and two in five mothers who breastfed at least initially (40%) said that they had done so while breastfeeding. At Stage 3, only a small minority of infants had been given peanuts or peanut products (8%).

431. Ninety percent of mothers completely avoided the use of salt in the diets of their eight to ten month old infants, but mothers from ethnic minority backgrounds were less likely to do so. Thirty-seven percent of mothers of “Chinese or other” ethnic origin, 37% of “Asian or British Asian” mothers, 26% of “Black and Black British” mothers and 16% of mothers of “Mixed” ethnic origin added salt to their infants’ diets, compared with only 5% of “White” mothers.

432. Nearly half of mothers mentioned that they avoided giving their infant particular ingredients at Stage 3 (45%). Other than salt, the principal ingredients omitted were nuts (41%), sugar (38%), honey (19%), eggs (12%) and dairy produce (11%).

Supplementary vitamins

433. The UK health departments have recommended for some time that children from six months to five years old should be given a supplement containing vitamins A, C and D, unless they are receiving more than 500 ml of infant formula per day (Department of Health, 1994; Department of Health and Social Security, 1988). The advice at the time of this survey was that if there was any doubt about the mother’s vitamin D status (for example, if she did not take a vitamin D supplement during her pregnancy or falls into other at-risk groups), breastfed infants were to be administered vitamin supplements from one month (Department of Health, 1998).

434. Seven per cent of infants at Stage 1 were being given vitamin drops, rising to 14% at Stage 3 (Table 10.13). As expected, breastfeeding mothers were more likely to be giving vitamin drops than those feeding with formula, particularly at Stage 3 (22% and 11% respectively).

The UK Diet and Nutrition Survey of Infants and Young Children (DNSIYC)

435. The UK Diet and Nutrition Survey of Infants and Young Children (DNSIYC) (Lennox et al., 2013) was commissioned by the Department of Health (DH) and the Food Standards Agency (FSA) to provide detailed information on the food composition, nutrient intakes and nutritional status of infants and young children aged four months up to eighteen months[48] living in private households in the UK. Fieldwork was carried out between January and August 2011.

436. DNSIYC provides the only source of high quality nationally representative data on the types and quantities of foods consumed by the 4 –

[48] Includes children aged up to 17 months and 28-31 days.

18 month age group. The Survey was conducted in all four countries of the UK and was designed to be representative of the UK population. Additional recruitment was undertaken in Scotland and among those in receipt to Healthy Start (HS) vouchers[49] in order to provide more detailed analysis of these populations. These additional samples were referred to as 'boosts'.

437. The survey involved a face-to-face interview to obtain background information, such as socio-economic status, a four-day food diary, and child and maternal anthropometric measurements. Information was obtained from 2,683 individuals, or 2,283 excluding the "Scottish boost". Nine hundred and seventy three infants attended a clinic at which 98% provided a measure of skinfold thickness, 87% completed a stable isotope assessment of fluid intake, breast milk intake and body composition and 55% provided a blood sample for the analyses of iron and vitamin D status.

Feeding patterns

438. Overall, feeding patterns observed in DNSIYC were very similar to those recorded by IFS 2010.

439. Seventy-eight per cent of the infants recruited had been breastfed at some point since birth, of which 57% were not breastfed beyond three months. Only two children (aged four to six months) were exclusively breastfed at the time of the survey.

440. Ten per cent of the infants in DNSIYC were introduced to complementary foods before the age of three months. Seventy-five per cent of infants consumed complementary foods before the age of five months and 22% were introduced at the age of six months. Baby rice and pureed fruit or vegetables were the most common first foods consumed by infants (65% and 21%, respectively).

441. Children aged less than one year generally consumed no more than 146g of whole milk per day.

442. The mean total fruit and vegetable consumption (which includes composite dishes) ranged from 100g per day for children aged four to six months to 170g per day for children aged 12 to 18 months. This equates to two adult (80g) portions per day. Mean fruit consumption of 7 – 18 month olds was 73 – 96g per day which was higher than that observed in the NDNS 11 – 18 year old Survey (62g per day).

[49] Healthy Start is a UK-wide government scheme set up to offer a nutritional safety net for pregnant women, new mothers and children under four years of age in very low income families, and encourage them to eat a healthier diet. The scheme provides vouchers to put towards the cost of milk, fruit and vegetables or infant formula, and coupons for free Healthy Start vitamin supplements.

443. The limited data on liver consumption indicate that frequent consumption (once a week or more) of liver and liver-containing products (for example, sausages) could lead to retinol intakes above the Tolerable Upper Level (TUL).

444. The proportion of children given a vitamin-mineral supplement during the four-day food diary period ranged from 5% (aged four to six months) to 10% (aged 12 to 18 months). Those most likely to receive at least one supplement were children aged 4 to 18 months of South Asian and ‘other’ ethnicities.

Nutrient intakes

445. Seventy-five percent of boys and 76% of girls exceeded the Estimated Average Requirement (EAR) for energy. Infant formula was the largest contributor to energy intake for children under twelve months of age.

446. Table 10.14 shows by infant age the percentage contribution of each food group to average daily energy intake. Between four and six months of age infant formula and breastmilk accounted for 69% of average daily energy intake, declining to 12% at twelve to eighteen months of age. Cereals/ cereal products and milk /milk products were the greatest contributors to energy intake after twelve months, together accounting for about half of daily energy intake.

447. After the first year of life cereals/ cereal products and milk /milk products were the principal dietary sources of non-milk intrinsic sugar (NMES). NMES accounted for 7.7% of energy intake at this age.

448. The proportion of children in all age groups, with mean daily intakes of vitamins below the Lower Reference Nutrient Intake (LRNI) was 8% or less. For vitamin A, 2% of children aged 12 – 18 months were below the LRNI. No children were below the LRNI for vitamin C (Table 10.15). Average daily intakes of all vitamins other than vitamin D exceeded RNI (Table 10.16).

449. The vitamin D intake of breastfed children from food and supplements was between 37 and 54% of Reference Nutrient Intake (RNI) at various ages, excluding any contribution from breastmilk. The mean daily intake of non-breastfed children exceeded RNI at all ages under twelve months (Table 10.16).

450. Infant formula was the largest contributor to vitamin A intake for the three youngest age groups (39%, 33% and 30% respectively).

451. Average daily intake of minerals from all sources generally exceeded RNI (Table 10.17) though intake of iron fell below the LRNI in 10 – 14% at all ages (Table 10.18). Infant formula was the major contributor to iron intake for children aged four to six months (56%), seven to nine months (48%) and ten to eleven months (42%).

452. Table 10.19a shows average daily intakes of sodium between 4 and 18 months of age. These exceeded the SACN guidance (2003), particularly after ten months of age. Table 10.19b shows the percentage contribution of food groups to daily sodium intake in children aged between 4 – 18 months.

Body size

453. More than 75% of the sample exceeded the WHO growth standard 50th percentile for weight, more than 70% for length and more than 79% for head circumference (Table 10.20).

Blood analytes

454. Iron status measures are shown in Table 10.21. Five children (3%) under 12-months of age satisfied the diagnostic criteria of IDA[50].

455. Ninety-four per cent of children (aged 5 to 11 months) had serum 25-hydroxyvitamin D (25-OHD) concentrations compatible with the SACN recommendation for good health (≥25nmol/l; SACN, 2016).

Conclusions

456. The five yearly infant feeding surveys have provided a unique perspective on infant feeding practices in the UK over the period 1975 – 2010. By using consistent methodology to survey a national sample they have documented in an unbiased manner the geographical, demographic, social and educational inequalities that underlie variations in infant nutrition and health.

457. The Surveys have shown increases in the proportion of women initiating breastfeeding, particularly since 2000 but the proportion of women who discontinue before the infant is six weeks old has remained between 30-39% since 1990.

[50] IDA was defined as those children below the lower threshold of population iron sufficiency for both age specific ferritin and haemoglobin. The base for haemoglobin has been used to calculate the percentage of children indicating IDA.

458. The proportion of women who breastfeed exclusively to six months of age or who continue to breastfeed beyond the first six months is very low compared with other high income countries.

459. There has been a reduction in the proportion of infants receiving solid foods before four months of age since 2000. This reflects a change in advice from the UK Health Departments during 2003.

460. Both IFS and DNSIYC have shown that the proportion of infants receiving vitamin supplements is low (less than 14%).

461. Despite this, there was a low prevalence of suboptimal serum vitamin D levels (6%) and only 2% of children aged12-18 months had intakes of vitamin A below the LRNI, while no children were below the LRNI at age 4-11 months

462. The main source of iron was consumption of infant formula and follow-on formula in the second six months of life, but only low prevalences of iron deficiency anaemia (3%) were found in DNSIYC.

463. Very low reliance on cows' milk as a main drink in the first year of life is reassuring.

464. Contrary to popular perception fruit and vegetable consumption in this age group is substantial and relatively higher than intake later in childhood.

465. Salt intakes in DNSIYC exceeded SACN guidance by 50-100% after 10-months of age.

Chapter 11. Risks of chemical toxicity in relation to the infant diet

466. To complement the SACN review of the scientific evidence underpinning current dietary recommendations for infants and young children in the United Kingdom, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) were asked to examine the risks of toxicity from chemicals in the diet of infants and to consider whether current Government advice should be revised. The COT was also tasked with assessing the evidence base relating to the influence of infant diet on development of food allergy, and atopic and auto-immune disease (see Chapter 12).

467. The COT reviewed the toxicity of a number of chemicals which were selected on the basis of their known or suspected adverse effects and the potential for dietary exposure for infants via breast milk, infant formulae, and complementary foods[51].

468. Consequently, COT published an overarching statement on risks of chemical toxicity and allergic disease in relation to the infant diet[52]. This included evaluations for caffeine, alcohol, methylmercury, dioxins and dioxin-like compounds, vitamin A, soy phytoestrogens, phthalates, bisphenol A, aluminium, lead, legacy pesticides, brominated flame retardants, and persistent organic pollutants. These are summarised in the Table 11.1.

469. In addition, COT decided that a more detailed review was required for a number of substances (vitamin A, aluminium, lead, soya phytoestrogens, brominated flame retardants, and environmental pollutants) and that these would be individually assessed and published as separate COT statements. These evaluations are summarised in Table 11.2 along with the links to these statements.

[51] https://cot.food.gov.uk/sites/default/files/cot/tox201203.pdf

[52] http://cot.food.gov.uk/sites/default/files/cot/cotstatementoverarch201203.pdf

Table 11.1: Summary of the substance evaluations included in the 2012 overarching statement on potential chemical risks from the infant diet.

Chemical considered	Summary of the COT conclusions on substances and contaminants[53]
Caffeine	Available information did not provide a basis for refining the advice that breastfeeding women should have no more than 200mg caffeine over the course of a day (which roughly equates to two mugs of instant coffee, or two mugs of tea, or one mug of filter coffee).
Alcohol	Evidence supported the recommendations that breastfeeding mothers should consume no more than 1 or 2 units of alcohol once or twice a week
Methylmercury	The exposure of infants to methylmercury from breast milk, infant formula and complementary foods did not exceed the safety guideline.
Dioxins and dioxin-like compounds	Dietary exposures of infants may exceed the safety guideline, but because this would only be for a short time, it would not be expected to produce a build-up in the body to levels that would be harmful. Furthermore, there was clear evidence from multiple studies that exposures were decreasing over time.
Phthalates	Exposures of infants to phthalates from breast milk, infant formula and complementary foods were found to be unlikely to exceed the safety guidelines.
Bisphenol A (BPA)	The exposures of infants to bisphenol A from breast milk, infant formula and complementary foods were well below the safety guideline. Moreover, exposures were likely to be even lower in the future as a result of decreased use of the chemical in plastic bottles used for infant feeding. The COT stated it would review its conclusions following the completion of the ongoing EFSA re-evaluation of BPA. *In 2015 EFSA published a new opinion on BPA, concluding that exposure estimates for infants and prenatally exposed children did not indicate a health concern.*
Legacy pesticides (including aldrin, dieldrin,endrin, chlordane, heptachlor, hexachlorobenzene, mirex, toxaphene, DDT)	These are a group of pesticides that were banned during the 1980s and 1990s, but which, because of their persistence in the environment, can still be detected in the food chain. The few studies that were available indicated that levels in breast milk were declining, and did not point to a concern for the health of UK infants.

[53] https://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2012/650147

Table 11.2: Summary of COT evaluations requiring more detailed assessment and the individual statement references.

Chemical considered	COT **conclusion**	**Reference / web link**
Soya phytoestrogens	There was some uncertainty about the safety of soya-based formula. The COT concluded that there was no scientific basis for a change in the government advice that there is no substantive medical need for, nor health benefit arising from the use of, soya-based infant formula and that it should only be used in exceptional circumstances to ensure adequate nutrition.	COT Statement on the potential risks from high levels of soya phytoestrogens in the infant diet (2013) http://cot.food.gov.uk/sites/default/files/cot/cotstatementoverarch201203.pdf
Aluminium	Estimated exposures to aluminium from dietary sources were considered to not indicate a toxicological concern or a need for modified Government advice.	COT Statement on the potential risks from aluminium in the infant diet (2013) http://cot.food.gov.uk/sites/default/files/cot/statealuminium.pdf
Lead	Total exposures to lead were unlikely to pose a material risk to health in the large majority of UK infants. However, there was a concern that adverse effects could occur where concentrations of lead in water or soil were unusually high.	COT Statement on the potential risks from lead in the infant diet (2013) http://cot.food.gov.uk/sites/default/files/cot/cotstatlead.pdf
Vitamin A	Overall the COT concluded that there was potential for some infants to exceed the tolerable upper limit (TUL) under the following circumstances: • if exclusively breastfed by mothers taking dietary supplements containing high levels of vitamin A, • if fed with infant formula at the upper limit of the retinol content allowed by regulation, • if given high dose vitamin A supplements • if consuming liver more than once per week The possibility of adverse effects from such exceedances could not be excluded, but should they occur, it was considered likely to be in only a very small proportion of infants.	COT Statement on the potential risks from high levels of vitamin A in the infant diet (2014) http://cot.food.gov.uk/sites/default/files/cot/cotstavita.pdf
Endosulfan isomers, pentachlorobenzene and chlordecone	Available information did not indicate a toxicological concern regarding dietary exposures to any of the three chemicals, since exposures were below the relevant safety guideline, or if none had been set, were low and decreasing.	COT Statement on endosulfan isomers, pentachlorobenzene and chlordecone in relation to infant diet. (2014) https://www.food.gov.uk/sites/default/files/cotstaonpops.pdf
α-, β- and γ-hexachloro-	Overall the COT concluded that its evaluation did not provide a basis for recommendations on	COT Statement on α-, β- and γ-

cyclohexanes (HCHs)	the infant diet relating to HCHs, particularly as levels in food appeared to be decreasing over time. However continued monitoring of HCHs in breast milk, infant formula and food, with appropriately sensitive methods, was considered useful to confirm that there are unlikely to be any risks.	hexachlorocyclohexanes in the infant diet (2014) http://cot.food.gov.uk/sites/default/files/cot/cotstatmhchs.pdf
Polybrominated biphenyls (PBBs)	Reliable estimation of infants’ exposure to PBBs was not possible, and thus no meaningful risk assessment could be performed.	COT Statement on polybrominated biphenyls (PBBs) in the infant diet (2015) http://cot.food.gov.uk/sites/default/files/pbbstatementfinal.pdf
Polybrominated diphenyl ethers (PBDEs)	Analysis indicated possible concerns regarding the exposures of infants to BDE-99 and -209 via ingestion of dust, to BDE-47, -99 and -153 via breast milk, and BDE-99 and -153 from food. Given that the main dietary sources of exposure to residual environmental PBDEs are breast milk and dairy products, COT considered the options for risk management were limited.	COT Statement on the potential risks from polybrominated diphenyl ethers (PBDEs) in the infant diet (2015) http://cot.food.gov.uk/sites/default/files/PBDEstatementfinal.pdf
Hexabromocyclo-dodecanes (HBCDDs)	Estimated exposures via breast milk and food were not a cause for concern, but high levels found in some samples of domestic dust were. Further dust sampling should be carried out to obtain a more reliable assessment of the distribution of potential exposures through ingestion of dust, and especially to establish whether levels begin to fall since production and new usage of HBCDDs has largely ceased. New studies on the levels of HBCDDs in infant formula and commercially produced infant food were also considered to be useful, but of lower priority.	COT Statement on the potential risks from hexabromocyclododecanes (HBCDDs) in the infant diet (2015) http://cot.food.gov.uk/sites/default/files/HBCDDsstatementfinal.pdf
Tetrabromobisphenol A (TBBPA)	COT concluded it was not possible to perform a meaningful risk assessment due to the lack of an appropriate reference point and limited exposure data.	No statement issued
Perfluorooctane sulfonate (PFOS)	Exposure estimates were found to be below the safety guideline, and even when allowance was made for any additional exposures to PFOS precursors, they did not indicate a need for formulation of dietary recommendations to protect the health of infants.	http://cot.food.gov.uk/sites/default/files/cot/cotstatmpfos.pdf
Acrylamide	The COT concluded that the low Margins of Exposure (MoEs[54]) from infants and young	COT Statement on potential risks from

[54] The margin of exposure (MOE) approach provides an indication of the level of health concern about a substance’s presence in food. EFSA’s Scientific Committee states that, for substances that are genotoxic and carcinogenic, an MOE of 10,000 or higher is of low concern for public health. The

	children's exposure to acrylamide from infant formula and food were a potential concern for genotoxicity and carcinogenicity. For other health effects such as neurotoxicity, exposures do not suggest any concern.	acrylamide in the diet of infants and young children (2016) https://cot.food.gov.uk/sites/default/files/finalacrylamidestatement.pdf
Arsenic	Overall, the inorganic arsenic exposures for exclusively breastfed or formula-fed UK infants aged 0 to 4 months generated MOEs that were generally greater than 10 and would therefore be considered of low concern. There could be a small risk to high level consumers of infant formula that has been reconstituted with water containing a high level of inorganic arsenic as this scenario generated MOEs that were marginally less than 10. Total exposure to inorganic arsenic, from dietary and non-dietary sources, in infants and young children aged 4 to 12 months and 1 to 5 years generally generated MOEs of less than 10 and could therefore pose a risk to health. When comparing the estimated exposures from different sources, it becomes apparent that in these age groups, dietary sources generally contribute more significantly to exposure than non-dietary sources such as soil and dust. It is therefore reiterated that efforts to reduce the levels of inorganic arsenic in food and water should continue.	Statement on potential risks from arsenic in the diet of infants aged 0 to 12 months and children aged 1 to 5 years (2016) https://cot.food.gov.uk/sites/default/files/finalstatementonarsenic_0.pdf

Conclusions

470. The COT assessed toxicity issues from the infant diet for a number of nutrients, substances and contaminants in breast milk, infant formulae, and solid foods. They concluded there were unlikely to be concerns over toxicity in the diet of infants for the majority of substances considered. Issues where there is potential concern are described in paragraphs 473 to 475.

471. In relation to vitamin A, COT concluded that there is potential for some infants to exceed the Tolerable Upper Limit (TUL) under the following circumstances:

- exclusively breastfed by mothers taking dietary supplements containing high levels of vitamin A;
- fed with infant formula at the upper limit of the retinol content allowed by regulation;
- given high dose vitamin A supplements;
- consuming liver more than once per week.

472. In relation to substances, COT concluded that:

margins of exposure identified in the Food Standard Agency's recent Total Diet Study on acrylamide range between 300 for an average adult consumer and 120 for toddlers.

- *Caffeine* - Breastfed infants can be exposed to caffeine as a result of maternal consumption of caffeine-containing foods and beverages, but the available scientific evidence does not demonstrate a consequent health risk in infants. The available information does not provide a basis for refining the current government advice that breastfeeding mothers should avoid drinking too much tea or coffee (only occasionally rather than every day).

- *Alcohol* - Reported effects in breastfed babies from maternal consumption of alcohol support the government's current advice that breastfeeding mothers should consume no more than 1 or 2 units of alcohol once or twice a week.

- *Soya* - There is some uncertainty about the safety of soya-based formula and there is no scientific basis for a change in the current government advice: there is neither substantive medical need for, nor health benefit arising from the use of soya-based infant formula and it should only be used in exceptional circumstances to ensure adequate nutrition.

- *Acrylamide* - There was a potential concern from exposure to acrylamide from infant formula and solid foods. Efforts to reduce acrylamide exposure should be continued, with respect to both commercially-produced and home-cooked food.

473. In relation to contaminants, COT concluded that:

- *Lead* - where soil and water concentrations of lead are unusually high there is concern that adverse effects could occur but that this is unlikely to pose a risk in the large majority of the UK.

- *Arsenic* - exposure for exclusively breastfed or formula-fed UK infants aged 0 to 4 months was considered of low concern. There could be a small risk to high level consumers of infant formula that has been reconstituted with water containing a high level of inorganic arsenic.

- *Polybrominated diphenyl ethers (PBDEs)* - no data were available on levels of PBDEs in infant formula and commercially produced infant foods in the UK. There are possible concerns in relation to PBDEs but dietary sources are residual environmental PBDEs in breast milk and dairy products with limited options for risk management.

Chapter 12. Risks arising from the infant diet and development of atopic and autoimmune disease

Background

475. Atopic conditions, including asthma, eczema, rhinitis and food allergy, appear to have increased in prevalence in recent decades in many countries, and are some of the commonest causes of chronic illness in children and young adults living in the UK (Gupta et al., 2004; 2007; Venter et al., 2010; De Silva et al., 2014; Nwaru et al., 2014). This apparent increase in disease prevalence, combined with data from migration studies, suggests that early-life environmental factors may be important modulators of allergic sensitisation and atopic disease risk. Similarly, the autoimmune diseases type I diabetes mellitus (TIDM) and Crohn's disease also appear to have increased in prevalence in some countries (Burisch & Munkholm, 2015; Patterson et al., 2012).

476. The relationship between maternal and infant dietary exposures and a child's risk of developing any of the common atopic and/or autoimmune diseases has been an area of considerable scientific uncertainty and debate in recent years.

477. The Committee on Toxicity of Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) was therefore asked to examine the evidence relating to the influence of infant diet on the development of food allergy, and atopic and auto-immune disease, to inform SACN's review of complementary feeding for infants. To support COT's considerations, the Food Standards Agency (FSA) commissioned Imperial College London to undertake a comprehensive systematic review of the published scientific literature in this area. The review was separated into three systematic reviews:

- Systematic review A: to explore the evidence relating to milk feeding and the child's future risk of developing allergic sensitisation, atopic disease, or autoimmune disease. This included the timing of transition from exclusive/predominant breastfeeding to partial or no breastfeeding in the first year of life, the total duration of breastfeeding up to 2 years of life and the timings of transition from liquid infant milk feed to complementary foods (other than infant formula) in the first year of life.

- Systematic review B: to explore the evidence concerning the timing of introduction of specific allergenic foods (cows' milk, hen's egg, peanut, tree nuts, fish, wheat, soya) into the infant diet during the first year of life and whether this influences the child's future risk of developing allergic sensitisation, atopic disease or autoimmune disease. This review also explored whether the observed effect varies according to exclusive/predominant and continued breastfeeding.

- Systematic review C: to explore the evidence that exposure to, or avoidance of, specific dietary patterns, food groups or nutrients, during the infants first year of life, during pregnancy or during lactation, influences the child's future risk of developing allergic sensitisation, atopic disease or autoimmune disease.

Types of studies to be included

478. The literature reviews only included evidence from human studies and focussed primarily on evidence derived from randomised controlled trials (RCTs), quasi RCTs, prospective cohort and longitudinal studies. Where data from prospective studies were limited or absent, retrospective cohort studies were included, as were nested case-control studies, other case-control studies and cross-sectional surveys.

479. Studies of infants between birth and 12 months of age were included in the review. Studies were excluded where participation was limited to infants with a specific disease state, premature infants <32 weeks gestation, or very low birth weight infants. Studies of infants at high risk of relevant outcomes on the basis of family or personal history or genotype were included.

480. Databases searched were The Cochrane Library; EMBASE; LILACS; MEDLINE and Web of Science, with the original searches run in July 2013 and updated in March 2016. PROSPERO was also searched for relevant systematic reviews. Existing and relevant systematic literature reviews published in the preceding two years were included and an independent quality scoring of any relevant systematic reviews was undertaken using the R-AMSTAR rating scale.

481. Studies were quality assessed using the Cochrane Risk of Bias tool for intervention trials, and the NICE methodological quality checklists for cohort and case control studies; with an additional assessment of risk of conflict of interest (Cochrane, 2009).

Outcome measures

482. Outcomes of interest were chosen for their prevalence in children and young adults, with a minimum inclusion criterion of 1 in 1000 prevalence in the general population. Atopic outcomes comprised: asthma / wheeze; atopic eczema; allergic rhinitis[55] ; food allergy; allergic sensitisation. Autoimmune outcomes

[55] In many studies, the definition of allergic rhinitis included "itchy, watery eyes" or allergic conjunctivitis.

comprised type 1 diabetes mellitus (TIDM); coeliac disease; inflammatory bowel disease (such as Crohn's disease and ulcerative colitis); autoimmune thyroid disease (such as Grave's disease or Hashimoto's thyroiditis); juvenile rheumatoid arthritis; vitiligo and psoriasis. Outcome data were analysed and presented within the age groups 0-4 years, 5-14 years and ≥15 years. Although analysis of studies of vitiligo and psoriasis were planned, no eligible studies were identified.

The COT review of atopic outcomes and autoimmune disease and the Joint SACN-COT working group statement

483. The commissioned systematic reviews have been evaluated by the COT (COT,2016)**,** and have been published in the peer-reviewed literature (Boyle et al, 2016; Ierodiakonou et al, 2016). The reviews considered many of the major food allergens (milk, hen's egg, fish, shellfish, tree nuts, wheat, peanuts and soya). The timing of introduction of fish (between six and twelve months) was found to be associated with the risk of developing allergic rhinitis, while the timing of introduction of gluten (between four to six months) was found to *not* increase the risk of coeliac disease. The reviews indicated that further consideration should be given to advice on the timing of the introduction of peanut and hen's egg into the infant diet.

484. A working group including members of SACN and COT was therefore convened to undertake a benefit-risk assessment relating to the timing of the introduction of peanut and hen's egg into the infant diet, and the risk of developing allergy to these foods. The joint working group has published a statement on its assessment .

Conclusions

485. There is insufficient evidence that the earlier introduction (than before around six months of age) of peanut or hen's egg would be beneficial to prevent the risk of allergy to the same foods, or that a 'window of opportunity' exists before six months of age.

486. Based on evidence relating to the consequences of reduced breast milk feeding, on the basis that complementary foods displace breast milk, introduction of complementary foods including peanut and hen's egg earlier than around six months of age presents risks that are not outweighed by any potential benefit.

487. Reasonable data exist to demonstrate that the deliberate exclusion or delayed introduction of peanut or hen's egg beyond six to twelve months of age may increase the risk of allergy to the same foods.

Chapter 13. Conclusions and recommendations

Background and context for the current review

488. The Committee on Medical Aspects of Food and Nutrition Policy (COMA) formulated guidance on infant feeding in a series of reports published since 1975. The last of these, "Weaning and the Weaning Diet" was published in 1994 (DH, 1994) and has remained the basis of much advice ever since.

489. A number of recommendations made by the Scientific Advisory Committee on Nutrition (SACN) and by international expert committees since the COMA 1994 review have carried implications for current infant feeding policy (for example, adoption of World Health Organization (WHO) Growth Standards (WHO MGRS 2006a, 2006b; SACN/RCPCH 2007) and revisions to energy requirements (FAO, 2004; SACN, 2011).

490. Breastfeeding, as the physiological norm, makes an important contribution to infant and lifelong health. Therefore, when considering evidence regarding the transition to solid feeding, the implications for breastfeeding must be considered. As any food other than breast milk taken before six months will tend to displace rather than supplement breast milk, the potential benefits of introducing any complementary food must be balanced against the risk of displacing breast milk**.**

Terms of Reference

491. The overarching aim of the current review is to reconsider the scientific basis of current recommendations for complementary and young child feeding up to five years of age.[56] This first report covers the infant period, from birth up to twelve months of age. In particular, the Committee was asked to consider evidence on developmental stages and other factors that influence eating behaviour and diversification of the diet[57], and to make recommendations. In keeping with SACN's terms of reference, only healthy term infants have been considered.

[56] The *early years* age group includes children aged from birth to five (define as until 31st August following their fifth birthday).

[57] *Diversification* of the diet refers to the progression from an exclusively milk-based diet to an eating pattern which includes a wide range of foods.

492. In parallel with SMCN, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) considered: a) the effects of early exposure to food antigens on the development of immune tolerance and b) exposure to food contaminants in breastmilk, commercially available infant foods and other constituents of the infant diet. COT Statements on these have been published separately[58].

Methodology

493. The SACN *Framework for the Evaluation of Evidence* (SACN, 2012) was used to identify and select appropriate evidence (published up to the end of 2015) for inclusion in the review. Consideration of the evidence was primarily focussed on prospective cohort studies, and randomised controlled trials where available, and on studies conducted in settings directly relevant to the United Kingdom.

494. Information on recent dietary patterns and nutritional status in infancy was derived from the five yearly Infant Feeding Surveys (IFS), which provided a unique perspective on infant feeding practices in the UK over the period 1975-2010 and from the Diet and Nutrition Survey of Infants and Young Children (DNSIYC).

495. Key outcomes indicating the adequacy of nutrient intake in infancy were considered to be the rate of linear growth and weight gain, and biochemical and haematological measures of nutritional status. The effects of not breastfeeding on infant and maternal morbidity were also considered. The Committee also considered how the infant’s neurological and developmental progression during the first year of life influences the acceptance of foods other than milk.

496. The Committee noted and took account of a number of limitations associated with infant feeding studies. Principally these were: inconsistent characterisation of the frequency and consistency of exposure to breastmilk; a paucity of randomised controlled trials; inadequate consideration of the strength and complexity of socio-demographic confounding; the rapid pace of change in the diet during the first year of life; and marked variability between infants in their rate of development.

Breastfeeding, growth and health

The conclusions in this section are based on the findings of Chapters 4 (Infant feeding, growth and health), 5 (Energy requirements), and 10 (UK Infant feeding practice)

[58] https://cot.food.gov.uk/committee/committee-on-toxicity/cotstatements

497. The WHO growth standard describes the linear and ponderal growth pattern of infants who are fully breastfed for the first six months of life. It prescribes a pattern of growth to be attained by all infants whether or not breastfed.

498. Breastfeeding has an important role in the development of the immune system through provision of passive specific and non-specific immune factors. There is strong epidemiological evidence that not breastfeeding is associated with an increased risk of hospital admission as a consequence of gastroenteritis or lower respiratory illness even in higher resource settings such as the United Kingdom.

499. Successive infant feeding surveys have shown increases in the proportion of women initiating breastfeeding, particularly since 2000 but the proportion of women who discontinue breastfeeding before the infant is six weeks old has remained at between 30-39% since 1990.

500. The proportion of women who breastfeed exclusively to six months of age (1%) or who continue to breastfeed beyond the first six months (34% at six months decreasing to <1% at one year) remains very low compared with other high income countries.

501. The early introduction of solid foods at three to four months is associated with greater risk of gastrointestinal, respiratory and ear infections than is continuing to breastfeed exclusively.

502. Continued breastfeeding alongside other foods throughout the first year is associated with improved infant and maternal health. Women who breastfeed for longer are at lower risk of breast cancer. Each additional year of breastfeeding during a woman’s lifetime is associated with a four per cent reduction in her lifetime risk of breast cancer.

503. Women who do not breastfeed, or do not breastfeed exclusively, show less postpartum weight loss than women who exclusively breastfeed, and there is evidence that the duration of breastfeeding is inversely associated with later maternal BMI.

504. Increasing the prevalence of breastfeeding would yield significant health service cost savings through reduction in the risk of common infections in infants including gastroenteritis, respiratory infections and otitis media.

505. The Estimated Average Requirement (EAR) for dietary energy in infancy is based on achievement of the growth pattern of infants exclusively or predominantly breastfed for around first six months of life. SACN’s recently

revised estimates of EAR for dietary energy of infants aged six to twelve months old (2011) are more than 15% lower than those previously set by COMA in 1991.

506. The best estimates to date indicate that breast milk production increases between four and six months and that this would meet the increasing energy demands of the growing infant. There is no evidence that breastfeeding exclusively for the first six months of life constrains energy intake or infant growth. A succession of randomised trials has shown that giving complementary foods to breastfed infants before six months compromises breastmilk intake without increasing total energy intake or increasing weight gain and is associated with other negative health outcomes.

Complementary feeding

The conclusions in this section are based on the findings of Chapters 6 (Infant feeding, body composition and health), 8 (Eating and feeding of solid foods) and 10 (UK infant feeding practice)

507. On average, infants are sufficiently neurologically mature to accept solid foods at around six months of age.

508. There has been a reduction in the proportion of infants receiving solid foods before four months of age since 2000. This reflects a change in advice from the UK Health Departments in 2003.

509. Patterns of infant feeding in the UK, including breastfeeding and age of introduction of solid foods, are strongly associated with social and educational status. This also applies to the age of introduction of solid foods and the quality of the complementary diet. Parents of breastfed infants are also more likely to follow complementary feeding guidance and other healthy lifestyle guidance.

510. These factors contribute to conflicting evidence, for example, some observational studies have described associations between the age of first complementary foods and later adiposity or obesity, but others have not. Several prospective studies have identified rapid early weight gain as a predictor rather than a consequence of the early introduction of solids indicating a likelihood of reverse causality in any relationship between early complementary feeding and subsequent overweight.

511. There are too few data to draw conclusions about relationships between age at introduction of complementary foods and cardio-metabolic outcomes in childhood or adult life. Two studies from the same UK cohort found weak associations between deviation from complementary feeding guidance and

diastolic blood pressure, but no effect of age at introduction of solids was apparent in another UK cohort or in several others from low-resource settings.

512. Introduction of complementary foods earlier than around six months of age presents risks that are not outweighed by any potential benefit. The existence of a sensitive or critical window for the acceptance of solid foods between four and six months has been hypothesised on the basis of observational evidence. However, findings from a randomised controlled trial did not support this hypothesis and indicated that introduction of complementary foods after six months was not associated with later difficulty in acceptance of solid foods.

513. There is experimental evidence that repeated exposure to new foods enhances acceptance and that offering a variety of foods helps to increase acceptance of new tastes.

514. The baby-led weaning approach to complementary feeding is as yet untested in a randomised controlled trial, but observational studies suggest that this approach may help infants accept a wider range of textures and flavours.

515. National survey data from DNSIYC indicate that while infants’ consumption of fruit and vegetables was fairly high (equivalent to two adult (80g) portions per day), salt (sodium chloride) intakes after ten months of age exceeded SACN guidance by 50-100%.

Micronutrients: Iron

The conclusions in this section are based on the findings of Chapter 7.

516. Iron status at birth is an important determinant of iron status throughout infancy, particularly the first six months of life. Cord blood ferritin concentrations are correlated with ferritin concentrations until at least two years of age.

517. Factors associated with lower iron status at birth include maternal iron deficiency anaemia, low birthweight and other indicators of pregnancy risk including obesity, smoking and gestational hypertension.

518. Delaying clamping of the umbilical cord until it has stopped pulsating (about three minutes after delivery) increases neonatal blood volume, red cell mass and therefore iron status at birth.

519. During the first six months of life exclusive breastfeeding provides sufficient dietary iron for healthy, term infants of appropriate weight born with adequate iron stores.

520. DNSIYC reported that the proportion of children with haemoglobin concentrations and serum ferritin concentrations below which iron deficiency anaemia is indicated was 3% for those aged five to eleven months.

521. There is substantial evidence that consumption of unmodified cows' milk is associated with low iron status in infants younger than twelve months of age. The low reliance on cows' milk as a main drink in the first year of life seen in DNSIYC offers reassurance that this risk is now better recognised.

522. Evidence on the effect of iron supplements on infant growth is mixed but there is evidence in infants who are iron replete that it may have a detrimental effect on linear growth and that it is not protective against future deficiency.

Micronutrients: Vitamins D and A

The conclusions in this section are based on the findings of Chapter 7.

523. Other than the prevention of nutritional rickets, data are not available to clearly relate serum 25(OH)D concentration in infants to current or long term non-skeletal health outcomes. Safe Intakes, based on a precautionary approach[59], rather than RNIs, are therefore recommended for infants and children aged up to four years. On this basis, a 'Safe Intake' of vitamin D is recommended in the range 8.5-10 µg/d (340-400 IU/d) for all infants from birth up to one year (whatever their mode of feeding) (SACN, 2016).

524. Both IFS and DNSIYC have shown that the proportion of infants receiving vitamin supplements was low (less than 14%), despite this being a universal recommendation.

525. In DNSIYC, only 2% of 12-18 month old children had intakes of vitamin A below the LRNI, while no child was below the LRNI (150µg retinol equivalents/day) at age four to eleven months.

526. The COT concluded that there is potential for some infants to exceed the Tolerable Upper Level (TUL) for vitamin A if "exclusively breastfed by mothers taking dietary supplements containing high levels of vitamin A" or if infants are "fed infant formula at the upper limit of the retinol content allowed by regulation, given high dose vitamin A supplements, or consume liver more than once per week." Since the TUL considers intakes over a lifetime, occasional intakes above

[59] COMA (DH, 1991) set a *'Safe Intake'* for some nutrients if there were insufficient reliable data to set DRVs. They are set on grounds of prudence and are *'judged to be a level or range of intake at which there is no risk of deficiency, and below a level of where there is a risk of undesirable effects'* (DH, 1991).

the TUL are unlikely to be of concern, however, as intake increases above the TUL, or if the excess intake is for a sustained period, the potential risk for adverse effects increases.

Oral health

The conclusions in this section are based on the findings of Chapter 9.

527. Current evidence suggests that breastfeeding, up to twelve months of age, is associated with a decreased risk of dental caries. Exclusive breastfeeding is the physiological norm for around the first six months of a child's life and has general and oral health benefits for the infant.

528. Consideration of children breastfed beyond twelve months was not within the remit of this report. However, conclusions drawn within the Tham et al (2015) systematic review suggest that an increased risk of dental caries once the primary teeth erupt may occur and be associated with factors such as breastfeeding *ad libitum* nocturnal feeding, and sleeping with the breast in the mouth. The authors acknowledged that the quality of most of these studies was judged as low, and with the exception of a single study in Brazil, confounders such as complementary feeding with cariogenic foods/drinks, or inadequate oral hygiene practices (for example, not brushing with a fluoride toothpaste) were not controlled for. Further research is required with careful control for confounding factors to inform infant feeding guidelines.

529. The one available systematic review found that 'ever breastfed' children appear to be less likely to develop a malocclusion in the primary dentition compared with 'never breastfed' children.

Risks arising from the infant diet and development of atopic and autoimmune disease

The conclusions in this section are based on the findings of Chapter 12.

530. There is insufficient evidence that the earlier introduction (than before around six months of age) of peanut or hen's egg would be beneficial to prevent the risk of allergy to the same foods, or that a 'window of opportunity' exists before six months of age.

531. Based on evidence relating to the consequences of reduced breast milk feeding, on the basis that complementary foods displace breast milk, introduction of complementary foods including peanut and hen's egg earlier than around six months of age presents risks that are not outweighed by any potential benefit.

532. Reasonable data exist to demonstrate that the deliberate exclusion or delayed introduction of peanut or hen’s egg beyond six to twelve months of age may increase the risk of allergy to the same foods.

Recommendations

533. The evidence reviewed for this report strengthens current guidance to breastfeed exclusively for around the first six months of the infant’s life and to continue breastfeeding throughout the first year. This makes an important contribution to infant and maternal health.

534. Greater focus should be given to reducing attrition rates and supporting women who make the informed choice to breastfeed for as long as possible, given the rapid decline in the proportion of women breastfeeding over the first few weeks of an infant's life. Increasing the proportion of women who continue to breastfeed or express breast milk beyond six months of age would yield additional health benefits.

535. Current advice that most infants should not start complementary foods until around the age of six months, having achieved developmental readiness, should continue. No infant should commence complementary feeding prior to four months of age.

536. First complementary foods should be encouraged from around six months of age and should include a wide range of foods and flavours, including iron- and calcium-containing foods.

537. Dietary and texture diversification should proceed incrementally throughout the complementary feeding period, taking into account the variability between infants in developmental attainment and the need to satisfy nutritional requirements. When introducing new foods it should be recognised that they may need to be presented on many occasions before they are accepted, particularly as infants get older.

538. In view of higher than recommended salt (sodium chloride) and sugar intakes in this age group, there is a need to re-emphasise the risks associated with adding salt and free sugars to infants’ food during the complementary feeding period.

539. To optimise iron status throughout the first year of life, NICE and SACN recommendations on delayed cord clamping should be implemented and monitored. Healthy infants of appropriate birthweight do not require iron

supplements. In keeping with current advice, cows’ milk should not be given as a main drink to infants under twelve months of age. Infants should be offered breastmilk, formula or water**.**

540. The low prevalence of vitamin A deficiency in the healthy infant population, despite the current low uptake of supplements, suggests the need to review recommendations on routine vitamin A supplementation.

541. The government should keep the risk from vitamin A, lead, soya-based formulas, acrylamide and arsenic under review. Efforts to reduce the levels of inorganic arsenic in food and water, and levels of acrylamide in commercially-produced and home-cooked foods should continue. In addition, government should consider opportunities to strengthen advice in relation to supplements and foods containing vitamin A. The use of soya-based formula should only be on medical advice.

542. Existing guidance relating to dental caries prevention in under three year olds includes:

- from six months of age infants should be introduced to drinking from a non-valve free-flowing cup to enable children to learn the skill of sipping, which is important in the development of the muscles used for talking. From age one year onwards, feeding from a bottle should be discouraged;
- sugar should not be added to complementary foods or drinks;
- the frequency and amount of sugary food and drinks should be reduced. Only plain milk or water should be provided between meals and offering baby juices or sugary drinks at bedtime should be discouraged.

543. Advice on complementary feeding should state that foods containing peanut and hen’s egg need not be differentiated from other complementary foods. Complementary foods should be introduced in an age-appropriate form[60] from around six months of age, alongside continued breastfeeding, at a time and in a manner to suit both the family and individual child.

544. The deliberate exclusion of peanut or hen’s egg beyond six to twelve months of age may increase the risk of allergy to the same foods. Once introduced, and where tolerated, these foods should be part of the infant’s usual diet, to suit both the individual child and family. If initial exposure is not continued as part of the infant’s usual diet, then this may increase the risk of sensitisation and subsequent

[60] Infants and young children should never be left alone while they are eating. Children under five years old must not be given whole nuts, as they can choke on them. Currently, it is advised that infants and young children should not eat raw eggs, eggs with runny yolks or any food that contains raw eggs and is uncooked or only lightly cooked. These can cause food poisoning and serious illness although this advice is currently under review as a result of the ACMSF recommendations (ACMSF, 2016). Eggs from other birds, such as duck, goose and quail eggs, should always be cooked thoroughly and this will not change following the current review.

food allergy. Families of infants with a history of early-onset eczema or suspected food allergy may wish to seek medical advice before introducing these foods.

545. There is a need to reinstate a form of national monitoring of the incidence and prevalence of breastfeeding, use of nutritional supplements, and use of foods other than breastmilk in infancy. The questions and definitions previously adopted in the five yearly Infant Feeding Survey should be used in order to allow tracking of secular trends and changes in practice consequent to new recommendations and guidance.

Research Recommendations

546. The intensity and duration of breastfeeding should be measured as precisely as possible in all studies, preferably by application of standard WHO definitions of breast milk exposure and a prospective study design. Definitions adopted should be fully explained in publications.

547. A control group with breastfeeding infants should be included, wherever possible, in studies considering alternative breastmilk substitutes or other infant dietary interventions [61].

548. Observational research should employ prospective data collection to minimise risk of reverse causation. Data should be collected with sufficient frequency to capture accurately and precisely the timing of events of interest, given the rapid pace of change in the infant diet.

549. It is important to control for potential confounding factors to accurately identify the impact of the diet and feeding practices at this crucial stage of development. Using a prospective cohort study design and gaining dietary intake data in the form of a diet diary will reduce the possibility of recall bias.

550. The strength and complexity of socio-demographic confounding of infant feeding practices, particularly in the United Kingdom, necessitates careful characterisation of study populations and exercise of considerable care when making statistical adjustment.

551. Growth outcomes in infant feeding studies should be related to the WHO multicentre growth study standards (2006) and those set by SACN/RCPCH (2007). Further research is required to monitor the quality of growth during infancy to distinguish between weight and length gain and accrual of lean body mass versus development of adiposity.

552. Research publications should describe the mode of delivery of drinks, for example, expressed breastmilk taken from a bottle and the use of free flow cups.

553. Research is required on the use of expressed breast milk on health outcomes, including oral health.

554. Further research is required to identify any association between breast and infant formula feeding and dental caries particularly after 12 months when the

[61] Committee on Medical Aspects of Food and Nutrition Policy. Guidelines on the nutritional assessment of infant formulas. Department of Health report on health and social subjects 47.: The Stationery Office, London (UK), 1996

consumption of other drinks, mixed feeding and toothbrushing habits are established.

555. There is a need to understand better the nature of caregiver responsiveness and the effect on the infant’s self-regulation of intake and weight gain. Interventional and longitudinal observational studies are required to determine more clearly the direction of causation.

556. Research is required into the cost effectiveness and benefit-risk of universal multivitamin supplementation in infancy as well as potential risks of voluntary multivitamin fortification of foods and drinks that are widely consumed in infancy.

557. Further research is required on the potential role of other micronutrients, not considered in this report.

558. Data on exposure to a number of potential contaminants is limited and the government should therefore consider the research requirements and outputs which would enable COT to draw effective conclusions on potential contaminants where current assessments were not able to be reliably made.

Glossary and abbreviations

Term	*Definition*
Birthweight	The weight of an infant at birth.
Body mass index (BMI)	An individual’s weight in kilograms divided by the square of height in metres (kg/m2). Often used as an indicator of adiposity with recognised limitations [Pietrobelli *et al.,* 1998].
Bottle-feeding	Feeding an infant from a bottle, whatever is in the bottle, including expressed breastmilk, water, formula, etc.
Cardiovascular disease	Cardiovascular disease is the most common cause of death in the UK and includes coronary heart disease (CHD), angina, heart attack and stroke.
Catch-up growth	Rapid growth following a period of restriction. Ultimately, it may redress wholly or partly the accrued deficit in weight or size though there may be consequences for body composition and metabolic capacity.
Cohort study	Systematic follow-up of a group of people for a defined period of time or until a specified event. Also known as a longitudinal study. A cohort study may collect data prospectively or retrospectively.
Complementary feeding	The World Health Organization (WHO) defines complementary feeding as ‘the process starting when breast milk alone is no longer sufficient to meet the nutritional requirements of infants” so that “other foods and liquids are needed, along with breast milk.” (WHO, 2002). For the purposes of this report, complementary feeding refers to the period when complementary foods are given in addition to either breast milk or breast milk substitutes. Complementary feeding replaces the term “weaning” which can be misinterpreted to mean the cessation of breastfeeding rather than the introduction of solid foods.

	Complementary foods are all liquids, semi-solid and solid foods, other than breast milk and breast milk substitutes
Diabetes	A metabolic disorder involving impaired metabolism of glucose due to either failure of secretion of the hormone insulin, *insulin-dependent or type 1 diabetes*, OR impaired responses of tissues to insulin, *non-insulin-dependent or type 2 diabetes*.
Diet and Nutrition Survey of Infants and Young Children (DNSIYC)	Survey providing detailed information on the food consumption, nutrient intakes and nutritional status of infants and young children aged 4 up to 18 months living in private households in the UK. Fieldwork was carried out between January and August 2011.
Diversification of the diet	*Diversification* of the diet refers to the progression from an exclusively milk-based diet to an eating pattern which includes a wide range of foods
Dual-energy X-ray absorptiometry (DEXA)	A technique used to measure bone mineral density.
Estimated Average Requirement (EAR)	Estimated Average Requirement of a group of people for energy or protein or a vitamin or mineral. About half of a defined population will usually need more than the EAR, and half less.
Exclusive breastfeeding	The WHO defines exclusive breastfeeding as no other food or drink, not even water, except breast milk) including milk expressed or from a wet nurse) for six months of life, but allows the infant to receive oral rehydration solutions (ORS), drops and syrups (vitamins, minerals and medicines. UK Health Departments recommend exclusive breastfeeding for the first six months of an infant's life [Department of Health, 2003].
Formula, Infant formula	A breastmilk substitute commercially manufactured to Codex Alimentarius or European Union standards.

Gestational age	The age of a fetus calculated from the first day of the mother's last menstrual period.
Head circumference	The circumference of the head measured at the level of the frontal and occipital prominences, its largest diameter.
Hypernatraemic dehydration	An abnormally high serum sodium concentration (>150mEq/l) caused by dehydration.
Infant	A child not more than twelve months (one year) of age.
Infant Feeding Survey (IFS)	The Infant Feeding Survey has been conducted every five years since 1975. The 2010 IFS was the eighth national survey of infant feeding practices to be conducted. The main aim of the survey was to provide estimates on the incidence, prevalence, and duration of breastfeeding and other feeding practices adopted by mothers in the first eight to ten months after their baby was born.
Intervention study	Comparison of an outcome (for example, disease) between two or more groups deliberately subjected to different exposures (for example, dietary modification or nutrient supplementation).
Longitudinal study	In a longitudinal study, individual subjects are followed through time with continuous or repeated monitoring exposures, health outcomes, or both.
Low birthweight (LBW)	Birthweight less than 2.5kg. Infants may be low birthweight because they are born too early or are unduly small for gestational age.
Lower reference nutrient intake (LRNI)	The estimated average daily intake of a nutrient which can be expected to meet the needs

	of only 2.5% of a healthy population. Values set may vary according to age, gender and physiological state (for example, pregnancy or breastfeeding).
Macronutrients	Nutrients that provide energy, including fat, protein and carbohydrate.
Meta-analysis	A quantitative pooling of estimates of effect of an exposure on a given outcome, from different studies identified from a systematic review of the literature
Micronutrients	Essential nutrients required by the body in small quantities, including vitamins and minerals.
Mixed feeding	An infant receives both breastmilk and infant formula. Complementary feeding (see above) is the process by which mothers give foods additional to breastmilk or infant formula
Nutrient deficiency	Impaired function due to inadequate supply of a nutrient required by the body.
Odds ratio (OR)	A measure of the risk of an outcome such as cancer, associated with an exposure of interest, used in case-control studies; approximately equivalent to the relative risk [World Cancer Research Fund / American Institute for Cancer Research, 2007].
Ponderal growth	A measure of leanness calculated as the relationship between mass and height (weight/length^3)
Randomised controlled trial (RCT)	A study in which eligible participants are assigned to two or more treatment groups on a random allocation basis. Randomisation assures the play of

	chance so that all sources of bias, known and unknown, are equally balanced.
Reference nutrient intake (RNI)	The average daily intake of a nutrient sufficient to meet the needs of almost all members (97.5%) of a healthy population. Values set may vary according to age, gender and physiological state (for example, pregnancy or breastfeeding).
Relative risk (RR)	The ratio of the rate of disease or death among people exposed to a factor, compared with the rate among the unexposed, usually used in cohort studies [World Cancer Research Fund / American Institute for Cancer Research, 2007].
Risk factor	A factor demonstrated in epidemiological studies to influence the likelihood of disease in groups of the population.
Solids	Foods other than breastmilk or formula milk introduced to the infant diet at the commencement of complementary feeding.
Systematic review	An extensive review of published literature on a specific topic using a defined search strategy, with a priori inclusion and exclusion criteria.
Tolerable Upper Level (TUL)	A tolerable upper intake level (TUL) is intended to specify the level above which the risk for harm begins to increase, and is defined as the highest average daily intake of a nutrient that is likely to pose no risk of adverse health effects for nearly all persons in the general population, when the nutrient is consumed over long periods of time, usually a lifetime.
Weaning	The process of expanding the diet to include foods and drinks other than breastmilk or infant

	formula [Department of Health, 1994]. The term complementary feeding is preferred to describe diversification of the diet because “weaning” has also been used to describe curtailment of breastfeeding.
Z-score	The Z-score (or standard deviation (SD) score) is defined as the difference between an observed value for an individual and the median value of the reference population, divided by the standard deviation value of the reference population. Z-scores are used for height, weight and head circumference.

References

Abdelrazik N, Al-Haggar M, Al-Marsafawy H, Abdel-Hadi H, Al-Baz R, Mostafa AH. Impact of long-term oral iron supplementation in breast-fed infants. *Indian Journal of Pediatrics* 2007; **74**(8):739-45.

Abraham EC, Godwin J, Sherriff A and Armstrong J. Infant feeding in relation to eating patterns in the second year of life and weight status in the fourth year. *Public Health Nutrition* 2012; **15**: 1705-1714

Abrams SA, Wen J, Stuff JE. Absorption of calcium, zinc, and iron from breast milk by five-to seven-month-old infants. *Pediatr Res* 1997;**41**: 384-90.

Adair LS, Fall CHD, Osmond C, Stein AD, Martorell R, Ramirez-Zea M, Singh Sachdev H, Dahly DL, Bas I, Norris SA, Micklesfield L, Hallal P, Victora CG, for the COHORTS group. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income: findings from five birth cohort studies. *Lancet* 2013; **382**: 525-34.

Adair L, Popkin BM, Vanderslice J, Akin J, Guilkey D, Black R *et al*. Growth dynamics during the first two years of life: a prospective study in the Philippines. *European Journal of Clinical Nutrition* 1993; **47**: 42-51.

Adlerberth I, Wold A E. Establishment of the gut microbiota in Western infants. *Acta Paediatr* 2009; **98**(2): 229-238.

Adu-Afarwuah S, Lartey A, Brown KH, Zlotkin S, Briend A, Dewey KG. Randomized comparison of 3 types of micronutrient supplements for home fortification of complementary foods in Ghana: effects on growth and motor development. *American Journal of Clinical Nutrition* 2007; **86**:412-20.

Aggett PJ, Agostoni C, Axelsson I, Bresson JL, Goulet O, Hernell O, Koletzko B, Lafeber HL, Michaelsen KF, Micheli JL, Rigo J, Szajewska H, Weaver LT. Iron metabolism and requirements in early childhood: do we know enough?: A commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr*ition 2002; **34**:337-45.

Agostoni C. *et al.* Medical position paper, Complementary feeding: A commentary by the ESPGHAN Committee on Nutrition. *Journal of Pediatric Gastroenterology and Nutrition* 2008; **46**: 99 – 110.

Ahn CH, MacLean WC Jr. Growth of the exclusively breast-fed infant. *European Journal of Clinical Nutrition.* 1980; **33**:183-92.

Akeson PMK, Axelsson IE, Raiha NCR. Growth and nutrient intake in three- to twelve- month old infants fed human milk or formulas with varying protein concentrations. *Journal of Pediatric Gastroenterology and Nutrition* 1998; **26**: 1-8.

Al-Dashti A, Williams S, Curzon M. Breast feeding, bottle feeding and dental caries in Kuwait, a country with low-fluoride levels in the water supply. *Community dental health* 1995;**12**(1): 42-47.

Alho OP, Laara E, Oja H. Public health impact of various risk factors for acute otitis media in northern Finland. *American Journal of Epidemiology* 1996;**143**(11):1149-56.

Alho OP, Laara E, Oja H. How should relative risk estimates for acute otitis media in children aged less than 2 years be perceived? *Journal of Clinical Epidemiology* 1996; **49**(1):9-14.

Allen, J. C., R. P. Keller, P. Archer and M. C. Neville. Studies in human lactation: milk composition and daily secretion rates of macronutrients in the first year of lactation. *American Journal of Clinical Nutrition* 1991; **54**(1): 69-80.

Al-Shehri S, Sweeney E, Cowley D, Liley H, Ranasinghe P, Charles B, Shaw P, Vagenas D, Duley J, Knox C. Deep sequencing of the 16S ribosomal RNA of the neonatal oral microbiome: a comparison of breast-fed and formula-fed infants.2016 Scientific Reports 6.

American Academy of Pediatric Dentistry. Definition of Early Childhood Caries (ECC); 2008. (http://www.aapd.org/assets/1/7/D_ECC.pdf.)

American Dental Association. From baby bottle to cup: Choose training cups carefully, use them temporarily. *Journal of the American Dental Association* 2004;**13**: 387.

American Dental Association. Tooth eruption. The primary teeth. *Journal of the American Dental Association* 2005;**136**: 1619.

Andersson O, Hellström-Westas L, Andersson D, Domellöf M. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. *British Medical Journal* 2011; 343.

Andersson O, Lindquist B, Lindgren M, Stjernqvist K, Domellöf M, Hellström-Westas L. Effect of delayed cord clamping on neurodevelopment at 4 years of age: a randomized clinical trial. *JAMA pediatrics*. 2015;**169**(7):631-8.

Arenz S, Ruckerl R, Koletzko B & von Kries R (2004). Breast-feeding and childhood obesity - a systematic review. *Int J Obes Relat Metab Disord* 2004; **28**: 1247-1256.

Aukett MA, Parks YA, Scott PH, Wharton BA. Treatment with iron increases weight gain and psychomotor development. *Archives of disease in childhood* 1986;**61**(9):849-57.

Avila, W. M., I. A. Pordeus, S. M. Paiva and C. C. Martins. Breast and bottle feeding as risk factors for dental caries: a systematic review and meta-analysis. *PloS one* 2015; **10**(11): e0142922.

Bachrach VR, Schwarz E, Bachrach LR. Breastfeeding and the risk of hospitalization for respiratory disease in infancy: a meta-analysis. *Arch Pediatr Adolesc Med* 2003; **157**(3): 237-243.

Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H & Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *British Medical Journal* 2005; **331**: 929.

Baird J, Poole J, Robinson S, Marriott L, Godfrey K, Cooper C, Inskip H, Law C; Southampton Women’s Survey Study Group. Milk feeding and dietary patterns predict weight and fat gains in infancy. *Paediatr Perinat Epidemiol* 2008; **22**: 575-586.

Baker JL, Michaelsen KF, Rasmussen KM & Sørensen TI. Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *American Journal of Clinical Nutrition* 2004; **80**: 1579-88.

Baker RD, Greer FR, The Committee on Nutrition. Clinical report – diagnosis and prevention of iron deficiency and iron deficiency anemia in infants and young children (0-3 years of age). *Pediatrics* 2010;**126**:1040-1050.

Barends C, de Vries JHM, Mojet J, de Graaf C. Effects of starting weaning exclusively with vegetables on vegetable intake at the age of 12 and 23 months. *Appetite* 2014; **81**: 193-199.

Barends C, de Vries JHM, Mojet J, de Graaf C. Effects of repeated exposure to either vegetables or fruits on infant’s vegetable and fruit acceptance at the beginning of weaning. *Food Quality and Preference* 2013; **29**: 157-165.

Bauchner H, Leventhal JM, Shapiro ED. Studies of Breast-feeding and Infections, How Good Is the Evidence?. *JAMA*. 1986; **256**(7):887-892.

Beal VA, Meyers AJ. Iron nutriture from infancy to adolescence. *American Journal of Public Health Nations Health*. 1970; **60**(4): 666-678.

Beauchamp GK, Mennella JA. Flavour perception in human infants: development and functional significance. *Digestion* 2011; **83**(suppl1): 1-6.

Beauchamp GK, Mennella JA. Early flavour learning and its impact on later feeding behaviour. *Journal of Pediatric Gastroenterology and* Nutrition 2009; **48**: S25-30.

Beauchamp GK, Mennella JA. Sensitive periods in the development of human flavor perception and preference. *Annales Nestle* 1998; **56**: 20-32.

Beauchamp GK, Cowart BJ & Moran M. Developmental changes in salt acceptability in human infants. *Dev Psychobiol* 1986; **19**: 17–25.

Beauchamp GK, Cowart BJ, Mennella JA, et al. Infant salt taste: developmental, methodogical, and contextual factors. *Dev Psychobiol* 1994; **27**: 353–365.

Behrendt, A., F. Sziegoleit, V. Muler-Lessmann, G. Ipek-Ozdemir and W. Wetzel. Nursing-bottle syndrome caused by prolonged drinking from vessels with bill-shaped extensions. *Journal of Dentistry for Children* 2001; **68**(1): 47-50, 12.

Birch LL, McPhee L, Shoba BC, Pirok E, Steinberg L. What kind of exposure reduces children’s food neophobia? Looking vs tasting. *Appetite* 1987; **9**:171-178.

Birch LL, Gunder L, Grimm-Thomas K, Laing DG. Infants’ consumption of a new food enhances acceptance of a new food enhances acceptance of similar foods. *Appetite* 1998; **30**: 283-295.

Birch LL, Fisher JO. Development of eating behaviours among children and adolescents. *Pediatrics* 1998; **101**: 539-549.

Birch LL, Marlin DW, Rotter J. Eating as the means activity in a contingency – effects on young childrens food preference. *Child Dev* 1984: **55**.

Blissett J. Relationships between parenting style, feeding style and feeding practices and fruit and vegetable consumption in early childhood. *Appetite* 2011;**57**:826-831.

Blisset J, Bennett C, Donohoe J, Rogers S, Higgs S. Predicting successful introduction of novel fruit to preschool children. *J Acad Nutr Diet* 2012;**112**:1959-67.

Blossfeld I, Collins A, Kiely M, Delahunty C. Texture preferences of 12 month old infants and the role of early experiences. *Food Quality and Preference* 2007; **18:** 396-404.

Bobrow KL, Quigley MA, Green J, Reeves GK, Beral V, Million Women Study Collaborators. Persistent effects of women's parity and breastfeeding patterns on their body mass index: results from the Million Women Study. *Int J Obes (Lond).* 2013;**37**(5):712-7.

Bowatte G, Tham R, Allen KJ, Tan DJ, Lau M1 Dai X, Lodge CJ. Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis. *Acta Paediatr.* 2015;**104**(467):85-95.

Brandtzaeg P. Development and basic machanisms of human gut immunity. *Nutrition Reviews* 1998; **56**, S5–S18.

Bramhagen AC, Axelsson I. Iron status of children in southern Sweden: effects of cow's milk and follow-on formula. *Acta Paediatrica* 1999;**88**(12):1333-7.

Brazionis L, Golley RK, Mittinty MN, Smithers LG, Emmett P, Northstone K and Lynch JW. Diet spanning infancy and toddlerhood is associated with child blood pressure at age 7.5 y. *American Journal of Clinical Nutrition* 2013; **97**: 1375-86.

Brion M-JA, Lawlor DA, Matijasevich A, Horta B, Anselmi L, Araújo CL, Menezes AMB, Victora CG and Davey Smith G. What are the causal effects of breastfeeding on IQ, obesity and blood pressure? Evidence from comparing high-income with middle-income cohorts. *International Journal of Epidemiology* 2011; **40**: 670-680.

Brown KH. The relationship between diarrhoeal prevalence and growth of poor infants varies with their age and usual energy intake (abstract). *FASEB Journal* 1991; **5**: A1079.

Brown A, Lee M. 2011. A descriptive study investigating the use and nature of baby-led weaning in a UK sample of mothers. *Matern Child Nutr* 2011; **7**: 34-47.

Brune M, Magnusson B, Persson H, Hallberg L. Iron losses in sweat. *American Journal of Clinical Nutrition* 1986; **43**:438-43.

Burdette HL, Whitaker RC, Hall WC & Daniels SR. Breastfeeding, introduction of complementary foods, and adiposity at 5 y of age. *American Journal of Clinical Nutrition* 2006; **83**: 550-8.

Burisch J and Munkholm P. The epidemiology of inflammatory bowel disease. *Scandinavian Journal of Gastroenterology* 2015; **50**: 942-951.

Butte NF: Energy requirements of infants. *Public Health Nutr* 2005;**8**:953– 67.

Cabrera-Rubio RMC, Collado K, Laitinen S, Salminen E, Isolauri A, Mira A. The human milk microbiome changes over lactation and is shaped by maternal weight and mode of delivery. *American Journal of Clinical Nutrition* 2012; **96**(3): 544-551.

Cameron N, Pettifor J, De Wet T, Norris S. The relationship of rapid weight gain in infancy to obesity and skeletal maturity in childhood. *Obesity Research* 2003; **11**: 457-460.

Cameron SL, Taylor RW, Heath AL. Parent-led or baby-led? Associations between complementary feeding practices and health-related behaviours in a survey of New Zealand families*. BMJ Open* 2013; **3**: e003946.

Capretta PJ, Petersik JT, Steward DJ. Acceptance of novel flavours is increased after early experience of diverse taste. *Nature* 1975;**254**:689-691.

Cardiff University. Picture of Oral Health: Dental Epidemiological Survey of 5 year olds 2014/2015; 2016.

Carruth BR, Ziegler PJ, Gordon A, Barr SI. Prevalence of picky eaters among infants and toddlers and their caregivers’ decisions about offering a new food. *J Am Diet.Assoc* 2004;**104**(1suppl 1):s57-s64.

Carruth BR, Skinner JD. Feeding behaviours and other motor development in healthy children (2-24 months). *J Am Coll Nutr* 2002;**21**(2):88-96.

Cashdan E. A sensitive period for learning about food. *Human Nature* 1994;**5**:279-291.

Castillo C, Atalah E, Riumallo J, Castro R. Breast-feeding and the nutritional status of nursing children in Chile. *Bulletin of the Pan American Health Organization* 1996; **30**: 125-33.

Caton SJ, Ahern SM, Remy E, Nicklaus S, Blundell P, Hetherington MM. Repetition counts: repeated exposure increases intake of a novel vegetable in UK pre-school children compared to flavour-flavour and flavour-nutrient learning. *British Journal of Nutrition* 2012; **30**: 1-9.

Caton SJ, Blundell P, Ahern SA, Nekising C, Olsen A, Møller P, Hausner H, Remy E, Nicklaus S, Chabanet C, Issanchou S, Hetherington MM. Learning to eat vegetables in early life: the role of timing, age and individual eating traits. *PLoS ONE* 2014;**9**(5): e97609.

Chambers TL, Steel AE. Concentrated milk feeds and their relation to hypernatraemic dehydration in infants. *Archives of Disease in Childhood* 1975**; 50**: 610.

Chantry CJ, Howard CR, Auinger P. Full breastfeeding duration and risk for iron deficiency in US infants. *Breastfeeding Medicine* 2007; **2**(2): 63-73.

Chantry, C. J., P. Auinger and R. S. Byrd. Lactation among adolescent mothers and subsequent bone mineral density. *Archives of Pediatrics and Adolescent Medicine* 2004;**158** (7): 650-6.

Chaparro CM, Neufeld LM, Tena AG, Eguia-Liz CR, Dewey KG. Effect of timing of the umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. *Lancet* 2006; **367** (9527): 1997-2004.

Chien PF, Howie PW. Breast milk and the risk of opportunistic infection in infancy in industrialized and non-industrialized settings. *Adv Nutr Res* 2001;**10**:69-104.

Chomtho S, Well JC, Williams JE, Davies PS, Lucas A, Fewtrell MS. Infant growth and later body composition: evidence from the 4-component model. *American Journal of Clinical Nutrition* 2008;**87**:1776-1784.

Claesson MJ, Cusack S, O'Sullivan O, Greene-Diniz R de Weerd H, Flannery E, Marchesi JR, Falush D, Dinan T, Fitzgerald G, Stanton C, van Sinderen D, O'Connor M, Harnedy N, O'Connor K, Henry C, O'Mahony D, Fitzgerald AP, Shanahan F, Twomey C, Hill C, Ross RP, O'Toole PW. Composition, variability, and temporal stability of the intestinal microbiota of the elderly. *Proceedings of the National Academy of Sciences of the United States of America* 2011; **108**: 4586-4591.

Cochrane Handbook for Systematic Reviews of Interventions; 2009. (http://handbook.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm)

Cohen RJ, Brown KH, Canahuati J, Rivera LL, Dewey KG. Effects of age of introduction of complementary foods on infant breast milk intake, total energy intake, and growth: a randomised intervention study in Honduras. *Lancet* 1994; **344**(8918): 288-93.

Cohen RJ, Rivera LL, Canahuati J, Brown KH, Dewey KG. Delaying the introduction of complementary food until 6 months does not affect appetite or mother's report of food acceptance of breast-fed infants from 6 to 12 months in a low income, Honduran population. *Journal of Nutrition* 1995; **125**(11):2787-92.

Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries including 50302 women with breast cancer and 96973 women without the disease. *Lancet* 2002; **20**: 187-95.

Cole TJ. Children grow and horses race: is the adiposity rebound a critical period for later obesity? *BMC Pediatrics* 2004; **4**: 6

Colomer J, Colomer C, Gutierrez D, Jubert A, Nolasco A, Donat J, Fernandez-Delgado R, Donat F, Alvarez-Dardet C. Anaemia during pregnancy as a risk factor for infant iron deficiency: report from the Valencia Infant Anaemia Cohort (VIAC) study. *Paediatric and perinatal epidemiology* 1990;**4**(2):196-204.

Cooke LJ, Wardle J, Gibson EL, Sapochnik M, Sheiham A, Lawson M. Demographic, familial and trait predictors of fruit and vegetable consumption by pre-school children. *Public Health Nutrition* 2004; **7**:295-302.

Cooke LJ. The importance of exposure for healthy eating in children: a review. *Journal of Human Nutrition and Dietetics* 2007; **20**: 294-301.

Cooke LJ, Fildes A. The impact of flavour exposure in utero and ruing milk feeding on food acceptance at weaning and beyond. *Appetite* 2011;**57**:808-811.

Capozzi L, Russo R, Bertocco F, Ferrara D, Ferrara M: Diet and iron deficiency in the first year of life: a retrospective study. *Hematology* 2010;**15**:410-413.

Coulthard H, Harris G, Emmett P. Delayed introduction of lumpy foods to children during the complementary feeding period affects child's food acceptance and feeding at 7 years of age. *Matern Child Nutr* 2009;**5**:75-85.

Coulthard H, Harris G, Fogel A. Exposure to vegetable variety in infants weaned at different ages. *Appetite* 2014; **78**C: 1-8.

Cox DR, Skinner JD, Carruth BR, Moran J, Houck KS. A food variety index for toddlers (VIT): development and application. *Journal of the American Dietetic Association* 1997; **97**(12); 1382-1386.
Cross, N. A., L. S. Hillman, S. H. Allen, G. F. Krause and N. E. Vieira. Calcium homeostasis and bone metabolism during pregnancy, lactation, and postweaning: a longitudinal study. *American Journal of Clinical Nutrition* 1995; **61**(3): 514-23.

Dallman PR, Widdowson EM, Dickerson JWT. Chemical composition of body. In: Comar CL, Bronner F, eds. Mineral metabolism: and advanced treatise volume 2 part A. *Orlando: Academic Press*, 1988: 1-247.

Daniels L, Heath AL, Williams SM, Cameron SL, Fleming EA, Taylor BJ, Wheeler BJ, Gibson RS, Taylor RW. Baby-Led Introduction to SolidS (BLISS) study: a randomized controlled trial of a baby-led approach to complementary feeding. *BMC Pediatr* 2015; **15**:179.

Danielsson, N., O. Hernell and I. Johansson. Human milk compounds inhibiting adhesion of mutans streptococci to host ligand-coated hydroxyapatite in vitro. *Caries research* 2009; **43**(3): 171-178.

Davidsson L, Galan P, Kastenmayer P, Cherouvrier F, Juillerat MA, Hercberg S, Hurrell RF. Iron bioavailability studied in infants: the influence of phytic acid and ascorbic acid in infant formulas based on soy isolate. *Pediatr Res* 1994; **36**:816-22.

Davies DP. Plasma osmolarity and feeding practices of healthy infants in first three months of life. *British Medical Journal* 1973; **2**: 340-342.

De Onis, M., Onyango, A., Borghi, E., Garza, C., & Yang, H. Comparison of the World Health Organization (WHO) Child Growth Standards and the National Center for Health Statistics/WHO international growth reference: Implications for child health programmes. *Public Health Nutrition* 2006;**9**(7), 942-947.

de Silva D, Geromi M, Halken S, Host A, Panesar SS, Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Cardona V, Dubois AEJ, Poulsen LK, Van Ree R, Vlieg-Boerstra B, Agache I, Grimshaw K, O'Mahony L, Venter C, Arshad SH and Sheikh A on behalf of the EAACI Food Allergy and Anaphylaxis Guidelines Group. Primary prevention of food allergy in children and adults: systematic review. *Allergy* 2014; **69**: 581–589.

Department of Health. Dietary Reference Values for Food, Energy and Nutrients in the United Kingdom. Report on Health and Social Subjects, No.41. London: HMSO; 1991.

Department of Health. Weaning and The Weaning Diet. Report on Health and Social Subjects, No.45. London: HMSO; 1994.

Department of Health. Guidelines on the nutritional assessment of infant formulas. A report of the Working Group on the Nutritional Assessment of Infant Formulas of the Committee on Medical Aspects of Food and Nutrition Policy. TSO; 1996.

Department of Child and Adolescent Health and Development/ Department of Nutrition for Health and Development/World Health Organization. Feeding the non-breastfed child, 6 – 24 months of age. Geneva: WHO; 2004.

Department of Health and Social Security: Present - day practice in Infant Feeding. Report of a Working Party of the Panel on Child Nutrition, Committee on Medical Aspects of Food Policy. London, HMSO; 1974

Department of Health and Social Security. Present - day practice in Infant Feeding. Report of a Working Party of the Panel on Child Nutrition, Committee on Medical Aspects of Food Policy.London, HMSO; 1980.

Department of Health and Social Security. Present Day Practice in Infant Feeding: Third Report. Report on Health and Social Subjects no.32. London, HMSO; 1988.

Department of Health. Nutrition and bone health: with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of the Food Nutrition Policy. London, The Stationery Office; 1998.

Department of Health. Scientific Review of the Welfare Food Scheme. Report on Health and Social Subjects no.51.London: The Stationery Office; 2002.

Desor JA, Maller O & Turner RE. Preference for sweet in humans: infants, children and adults. In Taste and Development: The Genesis of Sweet Preference, 161–172 [JM Weiffenbach, editor]. Washington, DC: US Government Printing Office; 1977.

Desor JA, Maller O & Turner RE. Taste in acceptance of sugars by human infants. *J Comp Physiol Psychol* 1973; **84**: 496–501.

Dewey KG, Cohen RJ, Rivera LL, Brown KH. Effects of age of introduction of complementary foods on iron status of breast-fed infants in Honduras. *Am J Clin Nutr* 1998; **67**: 878-84.

Dewey KG, Cohen RJ, Brown KH, Rivera LL. Age of introduction of complementary foods and growth of term, low-birth-weight, breast-fed infants: a randomized intervention study in Honduras. *American Journal of Clinical Nutrition* 1999; **69**:679-86.

Dewey KG, Domellöf M, Cohen RJ, Landa RL, Hernell O, Lonnerdal B. Iron supplementation affects growth and morbidity of breast-fed infants: results of a randomized trial in Sweden and Honduras. *J Nutr.* 2002; **132**:3249-55.

Dewey K. Guiding principles for complementary feeding of the breastfed child. Washington Pan American Health Organization/World Health Organization, Geneva; 2003.

DiSantis KI, Hodges EA, Johnson SL, Fisher JO. The role of responsive feeding in overweight during infancy and toddlerhood: a systematic review. *Int J Obes (Lond)* 2011; **35**(4): 480-92.

Domellöf M, Cohen RJ, Dewey KG, Hernell O, Rivera LL, Lönnerdal B. Iron supplementation of breast-fed Honduran and Swedish infants from 6 to 12 mo of age. *Am J Clin Nutr* 2001;**138**: 679-87.

Domellöf M, Lönnerdal B, Abrams SA, Hernell O. Iron absorption in breast-fed infants: effects of age, iron status, iron supplements, and complementary foods. *Am J Clin Nutr* 2002 **76**:198-204.

Domellöf M, Lönnerdal B, Dewey KG, Cohen RJ, Hernell O. Iron, zinc, and copper concentrations in breast milk are independent of maternal mineral status. *American Journal of Clinical Nutrition* 2004;**79**(1):111-115.

Domellöf M, Hernell O, Abrams SA, Chen Z, Lönnerdal B. Iron supplementation does not affect copper and zinc absorption in breastfed infants. *The American journal of clinical nutrition* 2009;**89**(1):185-90.

Domellöf M. Iron requirements in infancy. *Ann Nutr Metab* 2011**;59**:59-63.

Domellöf M, Braegger C,Campoy C, Colomb V, Decsi T, Fewtrell M, Hojsak I, Mihatsch W, Molgaard C, Shamir R, Turc D, van Goudoever J. Iron Requirements of Infants and Toddlers. *Journal of Pediatric Gastroenterology & Nutrition* 2014; **58** (1):119–129

Dovey TM, Staples PA, Gibson EL, Halford JCG. Food neophobia and ‘picky/fussy’ eating in children: A review. *Appetite* 2008; **50**: 181-193.

Drewett RF, Woolridge M. Milk taken by human babies from the first and second breast. *Physiology and Behavior* 1981 ;**26**(2) : 327-329.

Druet C, Stettler N, Sharp S, Simmons RK, Cooper C, Smith GD, Ekelund U, Lévy-Marchal C, Jarvelin MR, Kuh D, Ong KK. Prediction of childhood obesity by infancy weight gain : an individual-level meta-analysis. *Paediatr Perinat Epidemiol.* 2012 ; **26**(1) :19-26.

Du, M., Z. Bian, L. Guo, R. Holt, J. Champion and R. Bedi. Caries patterns and their relationship to infant feeding and socioeconomic status in 2-4-year-old Chinese children. *International Dental Journal* 2000; **50**: 385-389.

Duffy LC, Faden H, Wasielewski R *et al*. Exclusive breastfeeding protects against bacterial colonization and day care exposure to otitis media. *Pediatrics* 1997; **100**(4): E7.

Duijts L, Jaddoe VWV, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. *Pediatrics* 2010; **126**:e18.

Duncan B, Ey J, Holberg CJ *et al*. Exclusive breastfeeding for at least 4 months protects against otitis media. *Pediatrics* 1993; **91**(5): 867-72.

Durmuş B, Ay L, Duijts L, Moll HA, Hokken-Koelega AC, Raat H, Hofman A, Steegers EA & Jaddoe VW. Infant diet and subcutaneous fat mass in early childhood: the Generation R Study. *European Journal of Clinical Nutrition* 2012; **66**: 253–60.

Eaton-Evans J, Dugdale AE. Effects of feeding and social factors on diarrhoea and vomiting in infants. *Arch Dis Child* 1987; **62**:445.

Eriksson JG. Early growth and coronary heart disease and heart disease and type 2 diabetes: findings from the Helsinki Birth Cohort Study (HBCS). *American Journal of Clinical Nutrition* 2011;**94**:1799S-1802S.

European Society for Pediatric Gastroenterology Hepatology and Nutrition. Guidelines on Infant Nutrition. *Acta Paediatrica Scandinavica* 1982; Supplement 302.

European Food Safety Authority (EFSA). Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. *EFSA Journal* 2013;**11**(10):3408 [103 pp.].

Expert Group on Vitamins and Minerals (EVM). Safe Upper Level for Vitamins and Minerals. Expert Group on Vitamins and Minerals. 2003; P110-126. (https://cot.food.gov.uk/committee/committee-on-toxicity/cotreports/cotjointreps/evmreport)

Fall CHD, Borja JB, Osmond C, Richter L, Bhargava SK, Martorell R, Stein AD, Barros FC, Victora CG & the COHORTS group. Infant-feeding patterns and cardiovascular risk factors in young adulthood: data from five cohorts in low- and middle-income countries. *Int J Epidemiol* 2011;**40**: 47-62

Fein SB. Labiner-Wolfe J, Scanlon KS, Grummer-Strawn LM. Selected complementary feeding practices and their association with maternal education. *Pediatrics* 2008; **122**; S91-97.

Feldens, C., E. Giugliani, A. Vigo and M. Vitolo. Early feeding practices and severe early childhood caries in four-year-old children from southern Brazil: a birth cohort study.*Caries Research* 2010; **44**: 445-452.

Feldman R, Keren M, Gross-Rozvel , Tyano S. Mother-child touch patterns in infant feeding disorders: relation to maternal, child and environmental factors. *J Am Academy Child Adol Psychiatry* 2004;**43**(9): 1089-1097.

Fergusson DM, Horwood LJ, Shannon FT, Taylor B. Infant health and breast-feeding during the first 16 weeks of life. *Aust Paediatr J* 1978;**14**:254.

Fewtrell MS. The evidence for public health recommendations on infant feeding. *Early Human Development* 2011; **87**: 715-721.

Fewtrell MS, Wilson DC, Booth I, Lucas A. When to wean? How good is the evidence for six months’ exclusive breastfeeding. *British Medical Journal* 2011; **342**: 209-212.

Fewtrell MS, Morgan JB, Duggan C, Gunnlaugsson G, Hibberd PL, Lucas A, Kleinman RE. Optimal duration of exclusive breastfeeding: what is the evidence to support current recommendations? *American Journal of Clinical Nutrition* 2007; **85** (suppl1):635S-638S.

Field CJ. The immunological components of human milk and their effect on immune development in infants. *Journal of Nutrition* 2005; **135**:1-4.

Fildes A, Lopes C, Moreira P, Moschonis G, Oliveira A, Mavrogianni C, Manios Y, Beeken R, Wardle J, Cooke L. An exploratory trial of parental advice for increasing vegetable acceptance in infancy. *British Journal of Nutrition* 2015; **114** (2):328-36.

Fisk CM, Crozier SR, Inskip HM, Godfrey KM, Cooper C, Roberts GC, Robinson SM, the Southampton Women’s Survey Study Group. Breastfeeding and reported morbidity during infancy: findings from the Southampton Women’s Survey. *Maternal and Child Nutrition* 2011; **7**:61-70.

Flanagan PR. Mechanisms and regulation of intestinal uptake and transfer of iron. *Acta Paediatr Scand Suppl* 1989; **361**:21-30.

Fleischer Michaelsen K, Weaver L, Branca F & Robertson A. Feeding and nutrition of infants and young children. Guidelines for the WHO region with emphasis on the former Soviet countries. Geneva: WHO; 2000.

Fomon SJ. Potential renal solute load: considerations relating to complementary feedings of breastfed infants. *Pediatrics* 2000; **106**(Suppl 4): 1284.

Fomon SJ, Ziegler EE. Renal solute load and *potential* renal solute load in infancy. *J Pediatrics* 1999;**134**:11-14.

Fomon SJ, Ziegler EE, Nelson SE. Erythrocyte incorporation of ingested 58Fe by 56-day-old breast-fed and formula-fed infants. *Pediatr Res* 1993;**33**(6):573-576.

Fomon SJ, Filmer LJ Jr, Thomas LN, Anderson TA, Nelson SE. Influence of formula concentration on caloric intake and growth of normal infants. *Acta Paediatr Scand* 1975; **64**(2): 172-81.

Fomon SJ, Filer LJ, Thomas LN, Rogers RR, Proksh AM. Relationship between formula concentration and rate of growth of normal infants. *Journal of Nutrition* 1969; **98**: 241-54.

Food and Agriculture Organization. Requirements for Vitamin A, Iron, Folate and B12. Report of a Joint FAO/WHO Consultation. (Food and Nutrition Series No 23). Rome: FAO; 1988.

Food and Agriculture Organization and the World Health Organization. Human vitamin and mineral requirements. Report of a joint FAO/WHO expert consultation Bangkok, Thailand. Rome: WHO/FAO; 2002.

Food and Agriculture Organization. Human energy requirements. Report of a Joint FAO/WHO/UNU Expert Consultation no. 1. Rome: FAO; 2004.

Forestell CA, Mennella JA. Early determinants of fruit and vegetable acceptance. *Pediatrics* 2007; **120**(6):1247-1254.

Forestell CA, Mennella JA. More than just a pretty face. The relationship between infant's temperament, food acceptance, and mothers' perceptions of their enjoyment of food. *Appetite* 2012;**58**(3):1136-1142.

Fox, K. M., J. Magaziner, R. Sherwin, J. C. Scott, C. C. Plato, M. Nevitt and S. Cummings. Reproductive correlates of bone mass in elderly women. Study of Osteoporotic Fractures Research Group. *Journal of Bone and Mineral Research* 1993; **8**(8): 901-8.

Freeman VE, Mulder J, Van't Hof MA, Hoey HM, Gibney MJ. A longitudinal study of iron status in children at 12, 24 and 36 months. *Public health nutrition* 1998;**1**(2):93-100.

Frolich, A., M. Rudnicki, T. Storm, N. Rasmussen and L. Hegedus. Impaired 1,25-dihydroxyvitamin D production in pregnancy-induced hypertension. European Journal of Obstetrics, *Gynecology, and Reproductive Biology* 1992; **47**(1): 25-9.

Frongillo EA JR, de Onis M, Garza C, the WHO Task Force on Methods for the Natural Regulation of Fertility. Effects of timing of complementary foods on post-natal growth. Experimental Biology, New Orleans, April 1997. *FASEB Journal* 1997;**11**:A574.

Ganchrow JR, Steiner JE & Daher M. Neonatal facial expressions in response to different qualities and intensities of gustatory stimuli*. Infant Behav Dev* 1983; **6**: 473–484.

Gardiner PM, Nelson L, Shellhaas CS, Dunlop AL, Long R, Andrist S, Jack BW. The clinical content of preconception care: nutrition and dietary supplements. *Am J Obst Gyn* 2008;**199**(6 Suppl 2):S345–56.

Galloway AT, Lee Y, Birch LL. Predictors and consequences of food neophobia and pickiness in children. *Journal of the American Dietetic* Association 2003; **103**: 692-698.

Gasparoni A, Ciardelli L, Avanzini A, Castellazzi AM, Carini R, Rondini G, Chirico G. Age-related changes in intracellular TH1/TH2 cytokine production, immunoproliferative T lymphocyte response and natural killer cell activity in newborns, children and adults. *Biol Neonate*. 2003;**84**:297-303.

Gaur AH, Dominguez KL, Kalish ML, Rivera-Hernandez D, Donohoe M, Brooks JT et al . Practice of feeding premasticated food to infants: a potential risk factor for HIV transmission. *Pediatrics* 2009; **124**: 658-666.

Georgieff MK, Wewerka SW, Nelson CA. Iron status at 9 months of infants with low iron stores at birth. *The Journal of pediatrics* 2002;**141**(3):405-9.

Georgieff, M. K. Long-term brain and behavioral consequences of early iron deficiency. *Nutrition Reviews* 2011; **69**: S43–S48.

Gera T, Sachdev HP. Effect of iron supplementation on incidence of infectious illness in children: systematic review. *BMJ* 2002; **325**(7373):1142.

Gerrish C and Mennella J. Flavor variety enhances food acceptance in formula fed infants. *Am J Clin Nutr* 2001; **73**(6): 1080-1085.

Gertner, J. M., D. R. Coustan, A. S. Kliger, L. E. Mallette, N. Ravin and A. E. Broadus. Pregnancy as state of physiologic absorptive hypercalciuria. *American Journal of Medicine* 1986; **81**(3): 451-6.

Givens, M. H. and I. G. Macy. The chemical composition of the human fetus. *Journal of Biological Chemistry* 1933; **102**(1): 7-17.

Golley RK, Smithers LG, Mittinty MN, Emmett P, Northstone K and Lynch JW. Diet quality of UK infants is associated with dietary, adiposity, cardiovascular and cognitive outcomes measured at 7-8 years of age. *J Nutr* 2013; **143**: 1611-1617

Gondolf UH, Tetens I, Michaelsen KF, Trolle E. Dietary habits of partly breastfed and completely weaned infants at 9 months of age. *Public Health Nutrition* 2011;**15**(4):578-586.

Green R, Charlton R, Seftel H, Bothwell T, Mayet F, Adams B, Finch C, Layrisse M. Body iron excretion in man: a collaborative study. *Am J Med* 1968; **45**: 336-53.

Griffin IJ, Abrams SA. Iron and breastfeeding. *Pediatr Clin North Am* 2001; **48**: 1-13.

Grindefjord M, Dahllof G, Nilsson B, Modeer T. Prediction of dental caries development in one year old children. *Caries Research* 1995; **29**: 343-348.

Grote V, Schiess SA, Closa-Monasterolo R, Escribano J, Giovannini M, Scaglioni S, Stolarczyk A, Gruszfeld D, Hoyos J, Poncelet P, Xhonneux A, Langhendries JP, Koletzko B; European Childhood Obesity Trial Study Group. The introduction of solid food and growth in the first 2 y of life in formula-fed children: analysis of data from a European cohort study. *American Journal of Clinical Nutrition* 2011; **94**: 1785S-1793S.

Guignard JP. Renal function in the newborn infant. *Pediatr Clin North Am* 1982; **29**:777-790.

Gunnarsdottir I & Thorsdottir I. Relationship between growth and feeding in infancy and body mass index at the age of 6 years*. Int J Obes Relat Metab Disord* 2003; **27**: 1523–1527

Gunnarsson BS, Thorsdottir I, Palsson G. Iron status in 2-year-old Icelandic children and associations with dietary intake and growth. *Eur J Clin Nutr* 2004; **58**(6):901-6.

Günther ALB, Buyken AE, Kroke A. Protein intake during the period of complementary feeding and early childhood and the association with body mass index and percentage body fat at 7 y of age. *AJCN* 2007a;**85**:1626-1633.

Günther AL, Remer T, Kroke A, Buyken AE. Early protein intake and later obesity risk: which protein sources at which time points throughout infancy and childhood are important for body mass index and body fat percentage at 7 y of age? *Am J Clin Nutr* 2007b; **86**(6):1765-72.

Gupta R, Sheikh A, Strachan DP, Anderson HR. Burden of allergic disease in the UK: secondary analyses of national databases. *Clinical & Experimental Allergy* 2004; **34**(4): 520- 6.

Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007; **62**(1): 91-6.

Hanson LA. Breastfeeding provides passive and likely long-lasting active immunity. Ann Allergy Asthma Immunol 1998;**81**(6):523-33.

Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol* 2005;**162**: 397-403

Harris G. Developmental, regulatory and cognitive aspects of feeding disorders. In: Feeding problems in Children (eds. A. Southall & A. Schwartz) 2000;Radcliffe Medical Press: Oxford, UK.

Harvey NC, Robinson SM, Crozier SR, Marriott LD, Gale CR, Cole ZA, Inskip HM, Godfrey KM, Cooper C; Southampton Women's Survey Study Group. Breast-feeding and adherence to infant feeding guidelines do not influence bone mass at age 4 years. *British Journal of Nutrition* 2009; **102**(6): 15-20.

Haschke F & van't Hof MA. Euro-Growth references for breast-fed boys and girls: influence of breast-feeding and solids on growth until 36 months of age. *Journal of Pediatric Gastroenterology and Nutrition* 2000; **31**: S60–S71

Hausner H, Nicklaus et al. Breastfeeding facilitates acceptance of a novel dietary flavour compound. *Clinical Nutrition* 2010; **29**:141-148.

Havermans RC, Jansen A. Increasing children's liking of vegetables through flavour-flavour learning. *Appetite* 2007; **48**:259-262.

Hay G, Sandstad B, Whitelaw A, Borch-Iohnsen B. Iron status in a group of Norwegian children aged 6–24 months. *Acta Paediatrica* 2004; **93**: 592–598.

Hay G, Refsum H, Whitelaw A, Melbye EL, Haug E, Borch-Iohnsen B. Predictors of serum ferritin and serum soluble transferrin receptor in newborns and their associations with iron status during the first 2 y of life. *The American journal of clinical nutrition* 2007; **86**(1):64-73.

Haycraft E, Farrow C, Meyer C, Powell F, Blissett J. Relationships between temperament and eating behaviours in young children. *Appetite* 2011; **56**(3):389-392.

Health and Social Care Information Centre. National children's dental Health Survey:. Report 2: Dental Disease and Damage in Children: England, Wales and Northern Ireland; 2013. (http://content.digital.nhs.uk/catalogue/PUB17137.)

Health and Social Care Information Centre. Hospital Episode Statistics, Admitted Patient Care, England - 2013-14; 2015. (http://content.digital.nhs.uk/catalogue/PUB16719/hosp-epis-stat-admi-diag-2013-14-tab.xlsx.)

Heaney, R. P. and T. G. Skillman. Calcium metabolism in normal human pregnancy. *Journal of Clinical Endocrinology and Metabolism* 1971; **33**(4): 661-70.

Heath P, Houston-Price C, Kennedy OB. Increasing food familiarity without the tears. A role for visual exposure? *Appetite* 2011; **57**(3): 832-838.

Heath P, Houston-Price C, Kennedy OB. Let's look at leeks! Picture books increase toddlers' willingness to look at, taste and consume unfamiliar vegetables. *Frontiers in Psychology* 2014; **5** (191).

Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. Intake and growth of breast-fed and formula-fed infants in relation to the timing of introduction of complementary foods: the DARLING study. *Acta Paediatrica Scandinavica* 1993; **82**: 999-1006.

Hennessy MB, Smotherman WP, Levine S. Early olfactory enrichment enhances later consumption of novel substances. *Physiol Behav* 1977;**19**(4): 481-483.

Hetherington MM, Schwartz C, Madrelle J, Croden F, Nekitsing C, Verijken CMJL, Weenan J. A step-by-step introduction to vegetables at the beginning of complementary feeding. The effects of early and repeated exposure. *Appetite* 2015; 280-290.

Hetzner NM, Razza RA, Malone LM, Brooks-Gunn J. Associations among feeding behaviours during infancy and child illness at two years. *Maternal and Child Health Journal* 2009;**13**(6):795-805.

HM Government. Childhood Obesity: A Plan for Action; 2016. (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/546588/Childhood_obesity_2016__2__acc.pdf)

Hernell O, Fewtrell MS, Georgieff MK, Krebs NF, and Lönnerdal B.Summary of current recommendations on iron provision and monitoring of iron status for breastfed and formula-fed infants in resource-rich and resource-constrained countries. *The Journal of pediatrics* 2015; **167**(4): S40-S47.

Holgerson, P., N. Vestman, R. Claesson, C. Öhman, M. Domellöf, A. Tanner, O. Hernell and I. Johansson. Oral microbial profile discriminates breastfed from formula-fed infants. *Journal of pediatric gastroenterology and nutrition* 2013; **56**(2): 127.

Holgerson P, Harnevik L, Hernell O, Tanner AC, Johansson I. Mode of birth delivery affects oral microbiota in infants. *J Dent Res* 2011;**90**(10):1183-8

Hong, L., S. M. Levy, J. J. Warren and B. Broffitt. Infant breast-feeding and childhood caries: a nine-year study. *Pediatric dentistry* 2014;**36**(4): 342-347.

Hopkins D, Emmett P, Steer C, Rogers I, Noble S, Emond A. Infant feeding in the second months of life: an observational study. *Arch Dis Child* 2007; **92**: 850-854.

Hoppe C, Mølgaard C, Thomsen BL, Juul A & Michaelsen KF. Protein intake at 9 mo of age is associated with body size but not with body fat in 10-y-old Danish children. *AJCN* 2004; **79**: 494-501

Horta BL, Bahl R, Martines J, Victora C . Evidence on the long-term effects of breastfeeding: Systematic reviews and meta-analyses. World Health Organization: Geneva; 2007.

Horta BL &Victora CG. Long-term effects of breastfeeding: a systematic review. World Health Organization: Geneva; 2013. (http://apps.who.int/iris/bitstream/10665/79198/1/9789241505307_eng.pdf)

Howie PW, Forsyth JS, Ogston SA, Clark A, du V Florey C. Protective effect of breastfeeding against infection. *BMJ* 1990; **300**:11.

Huang MJ. An epidemiological study on prevalence and risk factors of hepatitis B virus (HBV) infection in preschool children. *Zhonghua Liu Xing Bing Xue Za zhi* 1990; **11**:129-32.

Huffman SL, Ford K, Allen HA, Streble P. Nutrition and fertility in Bangladesh: breastfeeding and post partum amenorrhea. *Population Studies* 1987;**41**:447–62.

Huh SY, Rifas-Shiman SL, Taveras EM, Oken E & Gillman MW. Timing of solid food introduction and risk of obesity in preschool-aged children. *Pediatrics* 2011; **127**: e544–e551.

Hulthen L, Lindstedt G, Lundberg PA & Hallberg L. Effect of a mild infection on serum ferritin concentration—clinical and epidemiological implications. *Eur. J. Clin. Nutr.* 1998. **52**:376–379.

Hurley KM, Cross MB, Hughes SO. A systematic review of responsive feeding and child obesity in high-income countries. *Journal of Nutrition* 2011; **141**(3): 495-501.

Idjradinata P, Watkins WE, Pollitt E. Adverse effect of iron supplementation on weight gain of iron-replete young children. *Lancet.* 1994; **343**(8908):1252-1254.

Illingworth RS, Lister J. The critical or sensitive period, with special reference to certain feeding problems in infants and children. *Journal of Pediatrics* 1964; **65**: 839-848.

Institute of Medicine (IOM). Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: National Academy Press; 2001.

Institute of Medicine (IOM). Dietary Reference Intakes for Vitamin D and Calcium. Editors: A Catharine Ross, Christine L Taylor, Ann L Yaktine, and Heather B Del Valle. Washington (DC): National Academies Press (US); 2011.
Ip S, Chung M, Raman G, *et al*. Breastfeeding and Maternal and Infant Health Outcomes in Developed Countries. Evidence Report/Technology Assessment Number 153. Agency for Healthcare Research and Quality, Rockville, MD; 2007.

Ip S, Chung M, Raman G, Trikalinos TA, Lau J. A summary of the Agency for the Healthcare Research and Quality’s evidence report on breastfeeding in developed countries. *Breastfeeding Medicine* 2009; **4**: S17-S30.

Jackson AA. Urea as a nutrient: bioavailability and role in nitrogen economy. *Arch Dis Child* 1994;**70**(1):3-4.

Jackson AA, Gibson NR, Bundy R, Hounslow A, Millward DJ, Wootton SA. Transfer of (15)N from oral lactose-ureide to lysine in normal adults. *Int J Food Sci Nutr* 2004; **55**(6):455-62.

Jackson DA, Imong SM, Wongsawasdii L, Silprasert A, Preunglampoo S, Leelapat P, Drewett RF, Amatayakul K, Baum JD. Weaning practices and breast-feeding duration in Northern Thailand. *Br J Nutr* 1992; **67**(2): 149-64.

Jaime-Perez JC, Herrera-Garza JL, Gomez-Almaguer D. Sub-optimal fetal iron acquisition under a maternal environment. *Archives of medical research* 2005; **36**(5):598-602.

Jeffery AN, Metcalf BS, Hosking J, Murphy MJ, Voss LD, Wilkin TJ. Little evidence for early programming of weight and insulin resistance for contemporary children: Early Bird Diabetes Study Report 19. *Pediatrics* 2006; **118**:1118-1123.

Johansson, I., Lif Holgerson P, Kressin, M. Nunn and A. Tanner . Snacking habits and caries in young children.*Caries research* 2010; **44**(5): 421-430.

Jonsdottir OH, Thorsdottir I, Hibberd PL, Fewtrell MS, Wells JC, Palsson GI, Lucas A, Gunnlaugsson G & Kleinman RE. Timing of the introduction of complementary foods in infancy: a randomized controlled trial. *Pediatrics* 2012; **130**: 1038–45.

Jontell M, Linde A. Nutritional aspects of tooth formation. *World Rev Nutr Diet* 1986;**48**:114–36. 17

Kajosaari M, Saarinen UM. Prophylaxis of atopic disease by six months’ total solid food elimination. Evaluation 135 exclusively breast-fed infants of atopic families. *Acta Paediatrica Scandinvaica* 1983; **72**:411-4.

Kalkwarf, H. J. Hormonal and dietary regulation of changes in bone density during lactation and after weaning in women. *Journal of Mammary Gland Biology and Neoplasia* 1999; **4**(3): 319-29.

Kent, G. N., R. I. Price, D. H. Gutteridge, K. J. Rosman, M. Smith, J. R. Allen, C. J. Hickling and S. L. Blakeman. The efficiency of intestinal calcium absorption is increased in late pregnancy but not in established lactation. *Calcified Tissue International* 1991; **48**(4): 293-5.

Kerstetter, J. E., A. C. Looker and K. L. Insogna. Low dietary protein and low bone density. *Calcified Tissue International* 2000; **66**(4): 313.

Kilbride J, Baker TG, Parapia LA, Khoury SA, Shuqaidef SW, Jerwood D. Anaemia during pregnancy as a risk factor for iron-deficiency anaemia in infancy: a case-control study in Jordan. *Int J Epidemiol* 1999; **28** (3): 461-468.

Kobayashi, A., S. Kawai, Y. Obe and Y. Nagashima. Effects of dietary lactose and lactase preparation on the intestinal absorption of calcium and magnesium in normal infants. *American Journal of Clinical Nutrition* 1975; **28**(7): 681-3.

Khadivzadeh T, Parsal S. Effect of exclusive breastfeeding and complementary feeding on infant growth and morbidity. *Eastern Mediterranean Health Journal* 2004;**10** (3):289–94.

Khan MU. Breastfeeding, growth and diarrhea in rural Bangladesh children. Human Nutrition. *Clinical Nutrition* 1984; **38**:113-9.

Khan KM, Krosch TC, Eickhoff JC, Sabati AA, Brudney J, Rivard AL, Foker JE. Achievement of feeding milestones after primary repair of long-gap esophageal atresia. *Early Human Development* 2009;**85**:387-392.

Kleinman RE. Pediatric nutrition handbook. Committee on Nutrition, American Academy of Pediatrics;1998.

Kleinman RE. Pediatric nutrition handbook. Committee on Nutrition, American Academy of Pediatrics. *Pediatrics* 2000; 106; 1274.

Kleinman RE. Pediatric nutrition handbook. Committee on Nutrition, American Academy of Pediatrics; 2003.

Knickmeyer RC1, Gouttard S, Kang C, Evans D, Wilber K, Smith JK, Hamer RM, Lin W, Gerig G, Gilmore JH. A structural MRI study of human brain development from birth to 2 years. *J Neurosci* 2008; **28**(47):12176-82.

Koletzko B, von Kries R, Closa R, Escribano J, Scaglioni S, Giovannini M, Beyer J, Demmelmair H, Gruszfeld D, Dobrzanska A, Sengier A, Langhendries JP, Rolland-Cachera MF & Grote V. Lower protein in infant formula is associated with lower weight up to age 2: a randomized clinical trial. *AJCN* 2009;**89**: 1836-1845.

Kovacs, C. S. and H. M. Kronenberg. Maternal-fetal calcium and bone metabolism during pregnancy, puerperium, and lactation. *Endocrine Reviews* 1997; **18**(6): 832-72.

Kovacs, C. S. Calcium and bone metabolism during pregnancy and lactation. *Journal of Mammary Gland Biology and Neoplasia* 2005; **10**(2): 105-18.

Kovacs, C. S. Vitamin D in pregnancy and lactation: maternal, fetal, and neonatal outcomes from human and animal studies. *American Journal of Clinical Nutrition* 2008; **88**(2): 520S-8S.

Kovacs, C. S. and H. M. Kronenberg. Pregnancy and lactation. In Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 7th Edition, edited by C. J. Rosen. Washington, DC: ASBMR Press. 2008; Pp. 90-5.

Kramer MS, Chalmers B, Hodnett ED, Sevkovskaya Z, Dzikovich I, Shapiro S *et al*. Promotion of breastfeeding intervention trial (PROBIT): a randomized trial in the Republic of Belarus. *JAMA* 2001;**285**:413-20.

Kramer MS, Matush L, Vanilovick I, Platt RW, Bogdanovich N, Sevkovskaya Z, Dzikovich I, Shisko G, Collet JP, Martin RM, Davey Smith G, Gillman MW, Chalmers B, Hodnett E, Shapiro S, PROBIT Study Group. Effects of prolonged and exclusive breastfeeding on child height, weight, adiposity and blood pressure at age 6.5y: evidence from a large randomized trial. *AJCN* 2007; **86**: 1717-21

Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database of Systematic Reviews* 2012, Issue 8. Art. No.: CD003517. DOI: 10.1002/14651858.CD003517.pub2.

Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database of Systematic Reviews* 2002, Issue 1. Art. No.: CD003517. DOI: 10.1002/14651858.CD003517.

Kramer MS, Vanilovich I, Matush L, Bogdanovich N, Zhang X, Shishko G, Muller-Bolla M, Platt RW. The effect of prolonged and exclusive breastfeeding on dental caries and school-age children. *Caries Res* 2007; **41**: 484-488.

Kramer MS, Guo T, Platt RW, Shapiro S, Collet JP, Chalmers B, Hodnett E, Sevkowskaya Z, Dzikovich I, Vanilovich I, PROBIT Study Group. Breastfeeding and infant growth: biology and bias? *Pediatrics* 2002;**110**(2 pt 1): 343-7).

Kuo ZY. The dynamics of behavior development: an epigenetic view. Random House, New York; 1967.

Labayen I, Ruiz JR, Ortega FB, Loit HM, Harro J, Villa I, Veidebaum T & Sjostrom M. Exclusive breastfeeding duration and cardiorespiratory fitness in children and adolescents. *AJCN* 2012; **95**: 498-505

Ladomenou F, Moschandreas J, Kafatos A, Tselentis Y, Galanakis E. Protective effect of exclusive breastfeeding against infections during infancy: a prospective study. *Arch Dis Child* 2010; **95**: 1004-1008.

Lange C, Visalli M, Jacob S, Chabanet C, Schlich P, Nicklaus S. Maternal feeding practices during the first year and their impact on infants' acceptance of complementary food. *Food Quality and Preference* 2013;**29**: 89-98.

Lartey A, Manu A, Brown KH, Peerson JM, Dewey KD. A randomized, community-based trial of the effects of improved, centrally processed complementary foods on growth and micronutrient status of Ghanaian infants from 6 to 12 mo of age. *Am J Clin Nutr* 1999; **70**:391-404.

Lawlor DA, Cooper AR, Bain C, Davey Smith G, Irwin A, Riddoch C & Ness A. Associations of birth size and duration of breast feeding with cardiorespiratory fitness in childhood: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Eur J Epidemiol* 2008; **23**: 411-22.

Lennox A, Sommerville J, Ong K, Henderson H, Allen R. Diet and Nutrition Survey of Infants and Young Children 2011; 2013. (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/139572/DNSIYC_UK_report_ALL_chapters_DH_V10.0.pdf)

Le Révérend BJD, Edelson LR, Loret C. Anatomical, functional, physiological and behavioural aspects of the development of mastication in early childhood. *Br J Nutrition* 2014; **111**: 403-414.

Ligh RQ, Fridgen J, Saxton C. The effect of nutrition and diet on dental structure integrity. *J Calif Dent Assoc.* 2001;**39**(4):243–9.

Lin SL, Leung GM, Lam TH, Schooling CM. Timing of solid food introduction and obesity: Hong Kong's "Children of 1997" birth cohort. *Pediatrics* 2013; **131**: e1459-67.

Lind T, Lönnerdal B, Stenlund H, Gamayanti IL, Ismail D, Seswandhana R, Persson LA. A community-based randomized controlled trial of iron and zinc supplementation in Indonesian infants: effects on growth and development. *Am J Clin Nutr* 2004; **80**(3):729-736.

Lindberg L, Bohlin G, Hagekull B. Early feeding problems in a normal population. *Int J Eating Disorders* 1991;**4**:395-405.

Litt MD, Reisine S, Tinanoff N. Multidimensional causal model of dental caries development in low-income preschool children. *Public Health Rep* 1995; **110**: 607-617.

Lönnerdal B, Keen CL, Hurley LS. Iron, copper, zinc, and manganese in milk. *Annu Rev Nutr* 1981; **1**:149-174.

Lönnerdal B. Nutritional and physiologic significance of human milk proteins. *Am J Clin Nutr* 2003;**77**(6):1537S-1543S.

Lozoff B & Georgieff MK. Iron Deficiency and Brain Development. *Seminars in Pediatric Neurology* 2006; **13**(3): 158-165,

Maier AS, Chabanet C, Schaal B, Issanchou SN, Leathwood PD. Effects of repeated exposure on acceptance of initially disliked vegetables in 7-month old infants. *Food Quality and Preference* 2007;**18**(8):1023-1032.

Maier AS, Chabanet C, Schaal B, Leathwood PD, Issanchou SN. Breastfeeding and experience with variety early in weaning increase infant's acceptance of new foods for up to two months. *Clinical Nutrition* 2008; **27**: 849-857.

Majumdar I, Paul P, Talib VH, Ranga S. The effect of iron therapy on the growth of iron-replete and iron-deplete children. *J Trop Pediatr*. 2003; **49**(2):84-88.

Makrides M, Leeson R, Gibson RA, Simmer K. A randomized controlled clinical trial of increased dietary iron in breast-fed infants. *J Pediatr* 1998; **133**:559-62.

Mallan KM, Daniels L, de Jersey SJ. Confirmatory factor analysis of the baby eating questionnaire and associations with infant weight, gender and feeding mode in an Australian sample. *Appetite* 2014; **82**: 43-49.

Male C, Persson LÅ, Freeman V, Guerra A, Hof MA. Prevalence of iron deficiency in 12-mo-old infants from 11 European areas and influence of dietary factors on iron status (Euro-Growth study). *Acta Paediatrica* 2001;**90**(5):492-8

Majorana, A., M. Cagetti, E. Bardellini, F. Amadori, G. Conti, L. Strohmenger and G. Campus. Feeding and smoking habits as cumulative risk factors for early childhood caries in toddlers, after adjustment for several behavioral determinants: a retrospective study. *BMC pediatrics* 2014; **14**(1): 45.

Marmot M, Bell R. Social determinants and dental health. *Advances in Dental Research* 2011; **23**, 201-206.

Marques TM, Wall R, Ross RP, Fitzgerald GF, Ryan CA, Stanton C. Programming infant gut microbiota: influence of dietary and environmental factors. *Current Opinion in Biotechnology* 2010; **21**(2): 149-156.

Marsh, P. and M. Martin. Oral Microbiology. Oxford, Wright; 1991.

Martin J. Infant feeding 1975: attitudes and practice in England and Wales. Office of Population Censuses and Surveys. London: HMSO;1978.

Martin J, Monk J. Infant feeding 1980. London: Office of Population Censuses and Surveys; 1982.

Martins S, Logan S, Gilbert RE. Iron therapy for improving psychomotor development and cognitive function in children under the age of three with iron deficiency anaemia. *Cochrane Database of Syst Rev* 2009. Issue 1.

Mason SJ, Harris G, Blissett J. Tube feeding in infancy. Implications for the development of normal eating and drinking skills. *Dysphagia* 2005; **20**: 46-61.

Mbulaiteye SM, Pfeiffer RM, Whitby D, Brubaker GR, Shao J, Biggar RJ. Human herpsevirus 8 infection within families in rural Tanzania *J Infect Dis* 2003; **187**:1780-5.

McAndrew F, Thompson J, Fellows L, Large A, Speed M, Renfrew MJ. Infant Feeding Survey 2010. Health and Social Care Information Centre. 2012. (http://content.digital.nhs.uk/catalogue/PUB08694/Infant-Feeding-Survey-2010-Consolidated-Report.pdf)

McDonald SJ, Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane database Syst Rev* 2008; (2): CD004074.

McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev* 2013; (7): CD004074.

McLean E, Cogswell M, Egli I, Wojdyla D, & De Benoist B.. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993–2005. *Public Health Nutrition* 2009;**12**(4), 444-454.

Mehta KC, Specker BL, Bartholmey S, Giddens J & Ho ML. Trial on timing of introduction to solids and food type on infant growth. *Pediatrics* 1998.**102**: 569–573

Mehta UJ, Siega-Riz AM, Herring AH, Adair LS & Bentley ME. Pregravid body mass index is associated with early introduction of complementary foods. *J Acad Nutr Diet* 2012; **112**: 1374-9

Mennella JA, Beauchamp GK. Maternal diet alters the sensory qualities of human milk and the nursling's behaviour. *Pediatrics* 1991;**88**(4):737-744.

Mennella JA, Beauchamp GK. Developmental changes in the acceptance of protein hydrolysate formula. *J Developmental and Behavaioural Pediatrics* 1996;**17**(6):386-391.

Mennella JA, Beauchamp GK. Mothers' milk enhances the acceptance of cereal during weaning. *Pediatr Res* 1997;**41**:188-192.

Mennella JA, Beauchamp GK. Development and bad taste. *Pediatr Asthma Allergy Immunol* 1998; **12**:161-163.

Mennella JA, Jagnow CP, Beauchamp GK. Prenatal and postnatal flavour learning by human infants. *Pediatrics* 2001;**107**(6):E88.

Mennella JA, Griffin BS, Beauchamp GK. Flavor programming during infancy. *Pediatrics* 2004;**113**:840-845.

Mennella JA, Beauchamp GK. Understanding the origin of flavour preferences. *Chem Senses* 2005; **30**(suppl 1): i242-i243.

Mennella JA, Nicklaus S, Jagolino Al, Yourshaw LM. Variety is the spice of life: strategies for promoting fruit and vegetable acceptance during infancy. *Physiol Behav.* 2008; **94**(1): 29-38.

Mennella J, Ventura A. Early Feeding: Setting the stage for healthy eating habits. Early Nutrition: Impact on short and long term health. *Nestle Nutr Inst Workshop Ser Pediatr Program* 2011; **68**:153-168. Basel.

Mennella J, Lukasewycz LD, Castor SM, Beauchamp GK. The timing and duration of a sensitive period in human flavor learning: a randomized trial. *Am J Clin Nutr* 2011; **93**: 1019-1024.

Mennella J, Trabulsi J. Complementary Foods and Flavour Experiences: Setting the foundation. *Ann Nutr Metab* 2012; **60** (suppl 2) 40-50.

Mennella J, Ziegler P, Briefel R, Novak T. Feeding Infants and Toddlers Study: the types of foods fed to Hispanic infants and toddlers. *J Am Diet Assoc* 2006;**106**:S96-S106.

Mennella J, Castor S. Sensitive period in flavour learning: effects of duration of exposure to formula flavors on food likes during infancy. *Clinical Nutrition* 2012; **31**: 1022-1025.

Mennella J, Forestell C, Morgan L, Beauchamp G. Early milk feeding influences taste acceptance and liking during infancy. *Am J Clin Nutr* 2009;**90**(suppl): 780S-8S.

Michaelsen, K, Thanh NM, Samuelson, G. (1995), A longitudinal study of iron status in healthy Danish infants: effects of early iron status, growth velocity and dietary factors. *Acta Pædiatrica* 1995; **84**: 1035–1044.

Mihrshahi S, Battistutta D, Magarey A, Daniels LA. Determinants of rapid weight gain during infancy: baseline results from the NOURISH randomised controlled trial. *BMC Pediatrics* 2011; **11**: 99.

Millward DJ, Forrester T, Ah-Sing E, Yeboah N, Gibson N, Badaloo A, Boyne M, Reade M, Persaud C, Jackson A. The transfer of 15N from urea to lysine in the human infant. *Br J Nutr* 2000; **83**(5): 505-12.

Moding K, Birch L, Stifter C. Infant temperament and feeding history predict infants' responses to novel foods. *Appetite* 2014; **83**: 218-225.

Monasta L, Batty GD, Cattaneo A, Lutje V, Ronfani L, van Lenthe FJ & Brug J. Early-life determinants of overweight and obesity: a review of systematic reviews. *Obesity Reviews* 2010; **11**: 695–708

Monteiro PO & Victora CG. Rapid growth in infancy and childhood and obesity in later life: a systematic review. *Obes Rev* 2005. **6**: 143-154

Moorcroft KE, Marshall JL & McCormick FM. Association between timing of introducing solid foods and obesity in infancy and childhood: A systematic review. *Maternal and Child Nutrition* 2011; **7**: 3–26

Morgan, M. and N. Monaghan. Picture Of Oral Health 2015: Dental Epidemiological Survey of 3 Year Olds In Wales 2013-14. Wales, Cardiff University & Public Health Wales; 2015.

Morton RE, Nysenbaum A, Price K. Iron status in the first year of life. *J Pediatr Gastroenterol Nutr* 1988;**7**(5):707-12.

National Institute for Health and Clinical Excellence (NICE). Intrapartum care. Care of healthy women and their babies during childbirth. NICE clinical guideline 55; 2007. (http://guidance.nice.org.uk/CG55/Guidance/pdf).

National Institute for Health and Clinical Excellence (NICE). Intrapartum care. Care of healthy women and their babies during childbirth. NICE clinical guideline 190; 2014. (https://www.nice.org.uk/guidance/cg190).

National Institute for Health and Care Excellence. Maternal and child nutrition: Public health guideline [PH11]; 2014. (http://www.nice.org.uk/guidance/PH11.)

National Health and Medical Research Council, Australian Government Department of Health and Ageing, New Zealand Ministry of Health. Nutrient Reference Values for Australia and New Zealand. Canberra: National Health and Medical Research Council; 2006.

NHS National Services Scotland. The National Dental Inspection Programme (NDIP): Report of the 2016 Detailed National Dental Inspection Programme of Primary 1 children and the Basic Inspection of Primary 1 and Primary 7 children; 2016.

Nehring I, Kostka T, von Kries R, Rehfuess EA. Impacts of in utero and early infant taste experiences on later taste acceptance: a systematic review. *J Nutr* 2015;1271-1279.

Nelle M, Zilow EP, Bastert G, Linderkamp O. Effect of Leboyer childbirth on cardiac output, cerebral and gastrointestinal blood flow velocities in full-term neonates. *Am J Perinatol.* 1995;**12**(3): 212-216.

Nelson, S. Wheeler's dental anatomy, physiology and occlusion, Elsevier Health Sciences; 2014.

Nicklaus S, Boggio V, Chabanet C, Issanchou S. A prospective study of food preferences in childhood. *Food quality and preference* 2004; **15**(7): 805-818.

Nicklaus S, V Boggio V, Chabanet C, Issanchou S. A prospective study of food variety seeking in childhood, adolescence and early adult life. *Appetite* 2005; **44**(3): 289-297.

Nicklaus S. Development of food variety in children. *Appetite* 2009; **52**: 253-255.

Nicklaus S. Children's acceptance of new foods at weaning. Role of practices of weaning and food sensory properties. *Appetite* 2011; **57**: 812-815.

Nielsen SB, Reilly JJ, Fewtrell MS, Eaton S, Grinham J, Wells JCK. Adequacy of milk intake during exclusive breastfeeding: a longitudinal study. *Pediatrics* 2011; **128**(4):e907-e914.

Northstone, K., Emmett, P., Nethersole, F. and the ALSPAC Study Team. The effect of age of introduction to lumpy solids on foods eaten and reported feeding difficulties at 6 and 15 months. *Journal of Human Nutrition and Dietetics* 2001; **14**: 43–54.

Northstone K, Emmett P, The ALSPAC Study Team. Multivariate analysis of diet in children at four and seven years of age and associations with socio-demographic characteristics. *Eur J Clin Nutr* 2005; **59**:751-760.

Norden. Nordic Nutrition Recommendations 2012, 5th edition; 2014 https://www.norden.org/en/theme/former-themes/themes-2016/nordic-nutrition-recommendation/nordic-nutrition-recommendations-2012

Nwaru BI, Hickstein L, Panesar SS, et al. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. *Allergy* 2014; **69**(8): 992-1007.

Oddy W, Holt P, Sly P, Read A, Landau L, Stanley F *et al*. Association between breast feeding and asthma in 6 year old children: findings of a prospective birth cohort study. *BMJ* 1999;**319**: 815-9.

Olausson H, Goldberg GR, Laskey MA, Schoenmakers I, Jarjou LMA, Prentice A. Calcium economy in human pregnancy and lactation. *Nutrition Research Reviews* 2012; **25**: 40-67.

Ollila P, Larmas M. A seven year survival analysis of caries onset in primary second molars and permanent first molars in different caries risk groups determined at age two years. *Acta Odontol Scand* 2007; **65**: 29-35.

Onayade AA, Abiona TC, Abayomi IO, Makanjuola ROA. The first six month growth and illness of exclusively and non-exclusively breast-fed infants in Nigeria. *East African Medical Journal* 2004;**81**(3):146–53.

Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *BMJ* 2000; **320**: 967-71

Ong KK & Loos RJ .Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr* 2006; **95**: 904-908

Oski FA. Iron requirements of the premature infant. In Tsang RC, ed. *Vitamin and Mineral Requirements in Preterm Infants.* New York: Marcel Dekker, 1985:9-21.

Pasricha SR, Flecknoe-Brown SC, Allen KJ, Gibson PR, McMahon LP, Olynyk JK, Roger SD, Savoia HF, Tampi R, Thomson AR, Wood EM & Robinson KL. Diagnosis and management of iron deficiency anaemia: a clinical update. *Med J Aust* 2010; **193**(9):525-32.

Paricio Talayero JM, Lizan-Garcia M, Otero Puime A, Benlloch Muncharaz MJ, Beseler Soto M, Sanchez-Palomares M, Santos Serrano L, Landa Rivera L. Full breastfeeding and hospitalization as a result of infections in the first year of life. *Pediatrics* 2006; **118**:e92-e99.

Patterson CC, Gyürüs E, Rosenbauer J, et al. Trends in childhood type 1 diabetes incidence in Europe during 1989-2008: evidence of nonuniformity over time in rates of increase. *Diabetologia* 2012; **55**(8):2142-2147.

Parkinson KN, Pearce MS, Dale A, Reilly JJ, Drewett RF, Wright CM, Relton CL, McArdle P, Le Couteur AS, Adamson AJ. Cohort Profile: The Gateshead Millennium Study. *Int J Epidemiol* 2011; **40** (2): 308-317.

Pearce J, Taylor MA, Langley-Evans SC. Timing of the introduction of complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013;**37**(10): 1295-1306.

Pearce J &Langley-Evans SC. The types of food introduced during complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013; **37**(4):477-85.

Pedersen, E. B., P. Johannesen, S. Kristensen, A. B. Rasmussen, K. Emmertsen, J. Moller, J. G. Lauritsen and M. Wohlert. 1984. Calcium, parathyroid hormone and calcitonin in normal pregnancy and preeclampsia. *Gynecologic and Obstetric Investigation* 1984; **18**(3): 156-64.

Pena-Rosas JP, Viteri FE. Effects and safety of preventive oral iron or iron+folic acid supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2009; (4):CD004736.

Persson LÅ, Lundström M, Lönnerdal B, Hernell O. Are weaning foods causing impaired iron and zinc status in 1-year-old Swedish infants? A cohort study. *Acta Paediatrica* 1998;**87**(6):618-22.

Peres KG, Cascaes AM, Nascimento GG, Victora CG. Effect of breastfeeding on malocclusions: a systematic review and meta-analysis. *Acta Paediatrica* 2015;**104**(S467): 54-61.

Perrotta, S., Novili, B., Rossi, F., Di, P, D., Cucciolla, V., Borriello, A., Oliva, A., Della R,F. Vitamin A and infancy. Biochemical, functional, and clinical aspects. *Vitam Horm* 2003; **66**:457-591.

Phatak A & Phatak P. Development of Indian babies and its assessment. Textbook of paediatrics. New Delhi: Jaypee Brothers 126-36; 1991.

Pisacane A. Neonatal prevention of iron deficiency. *BMJ* 1996; **312**; 136-137.

Pisacane A, De Vizia B, Valiante A, Vaccaro F, Russo M, Grillo G, Giustardi A. Iron status in breast-fed infants. *J Pediatr* 1995; **127**: 429-31.

Plagemann A & Harder T (2005). Breast feeding and the risk of obesity and related metabolic diseases in the child. *Metab Syndr Relat Disord* **3**: 222-232

Pliner P, Salvy SJ. Food neophobia in humans. In R. Shepherd & M.Raats (Eds.). The psychology of food choice; 75-92. Oxfordshire, UK: CABI Head Office; 2006.

Pokhrel S, Quigley MA, Fox-Rushby J, McCormick F, Williams A, Trueman P, Dodds R, Renfrew MJ. Potential economic impacts from improving breastfeeding rates in the UK. *Arch Dis Child* 2014; **100**:334-340.

Prentice, A. Micronutrients and the bone mineral content of the mother, fetus and newborn. *Journal of Nutrition* 2003; **133**(5 Suppl 2): 1693S-9S.

Prospective Studies Collaboration, Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, Qizilbash N, Collins R, Peto R. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009;**373**(9669):1083-96.

Public Health England. Delivering Better Oral Health: An evidence-based toolkit for prevention (Third Edition). London; 2014.

Public Health England. National Dental Epidemiology Programme for England: oral health survey of five-year-old children 2015. A report on the prevalence and severity of dental decay; 2016.

Public Health Wales.Bump, Baby & Beyond (version 2, 2015); 2014: http://www.wales.nhs.uk/documents/Pregnancy%20to%204%20Years%20Book%20FINAL%20English%20Revised%20E-Book%20Compressed.pdf

Qadri, G., A. Nourallah and C. Splieth. Early childhood caries and feeding practices in kindergarten children.*Quintessence International* 2012; **43**: 503-510.

Quigley MA, Cumberland P, Cowden JM, Rodrigues LC. How protective is breast feeding against diarrhoeal disease in infants in 1990? A case-control study. *Arch Dis Child* 2006; **91**:245-250.

Quigley MA, Kelly YJ, Sacker A. Infant feeding, solid foods and hospitalisation in the first 8 months after birth. *Arch Dis Child* 2009; **94**: 148-150.

Quigley MA, Kelly YJ, Sacker A. Breastfeeding and hospitalisation for diarrheal and respiratory infection in the United Kingdom Millennium Cohort Study. *Pediatrics* 2007; **119**:e837.

Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev*. 2012;**8**:

Ramakrishnan U, Nguyen P, Martorell R. Effects of micronutrients on growth of children under 5 y of age: meta-analyses of single and multiple nutrient interventions. *The American journal of clinical nutrition* 2009; **89**(1):191-203.

Rapley G. Baby-led weaning: transitioning to solid foods at the baby's own pace. *Community Practice* 2011;**84**(6): 20-3.

Rao R, Georgieff MK. Iron in fetal and neonatal nutrition. InSeminars in fetal and neonatal medicine 2007; **12**,(1),pp. 54-63. WB Saunders.

Rao S, Kanade AN. Prolonged breast-feeding and malnutrition among rural Indian children below 3 years of age. *European Journal of Clinical Nutrition* 1992; **46**: 187-95.

Rasmussen KM. Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *J Nutr* 2001;**131**:590S-603S.

Reilly JJ, Ashworth S, Wells JC. Metabolisable energy consumption in the exclusively breast-fed infant aged 3-6 months from the developed world: a systematic review. *Br J Nutr* 2005; **94**(1):56-63.

Reilly JJ, Wells JC. Duration of exclusive breastfeeding: introduction of complementary feeding may be necessary before 6 months of age. *Br J Nutr* 2005; **94**(6):869-872.

Remington JS, Klein JO. Developmental immunology and role of host defenses in fetal and neonatal susceptibility to infection. *Infectious diseases of the fetus and newborn infant, 6th ed*. Philadelphia: W.B. Saunders; 2006.

Remy E, Issanchou S, Chabanet C, Nicklaus S. Repeated exposure of infants at complementary feeding to a vegetable puree increases acceptance as effectively as flavor-flavor learning and more effectively than flavor-nutrient learning. *J Nutr* 2013; **143**(7):1194-200.

Renfrew MJ, Pokhrel S, Quigley M, McCormick F, Fox-Rushby J, Dodds R, Duffy S, Trueman P, Williams A. Preventing disease and saving resources: the potential contribution of increasing breastfeeding rates in the UK. London: UNICEF UK; 2012.

Renfrew MJ, Ansell P, Macleod KL. Formula feed preparation: helping reduce the risks; a systematic review. *Arch Dis Child.* 2003;**88**(10):855-8.

Retnakumari, N. and G. Cyriac. Childhood caries as influenced by maternal and child characteristics in pre-school children of Kerala-an epidemiological study. *Contemporary clinical dentistry* 2012; **3**(1): 2.

Robinson S, Crozier SR, Marriott L, Harvey N, Inskip HM, Godfrey K & Cooper. Protein intake in infancy is not associated with adiposity at 4 years of age: findings from the Southampton Women’s Survey. *Proc Nutr Soc* 2008; **67** (OCE8): E347

Robinson SM, Marriott LD, Crozier SR, Harvey NC, Gale CR, Inskip HM, Baird J, Law CM, Godfrey KM, Cooper C; Southampton Women's Survey Study Group. Variations in infant feeding practice are associated with body composition in childhood: a prospective cohort study. *J Clin Endocrinol Metab* 2009; **94**: 2799-805

Robinson S, Marriott L, Poole J, Crozier S, Borland S, Lawrence W, Law C, Godfrey K, Cooper C, Inskip H, SWS Study Group. Dietary patterns in infancy: the importance of maternal and family influences on feeding practice. *Br J Nutr* 2007; **98**: 1029-1037.

Rosado JL. Separate and joint effects of micronutrient deficiencies on linear growth.

Robson WL, Leung AK. The use of cow’s milk in infancy. *Pediatrics* 1993; **91**(2):515-516.

Rolland-Cachera MF, Deheeger M, Bellisle F, Sempé M, Guilloud-Bataille M, Patois E. Adiposity rebound in children: a simple indicator for predicting obesity. *AJCN* 1984; **39**: 129-135

Rosenstein D, Oster H. Differential facial responses to 4 basic tastes in newborns. *Child Development* 1988; **59** (6): 1555-1568.

Rozin P. The selection of food by rats, humans, and other animals. In J.S. Rosenblatt, R.A.Hindle, E. Shaw & C.Beer (Eds), *Advances in the study of behaviour* 1976; Pp. 21-76. New York: Academic Press.

Sachdev H, Gera T, Nestel P. Effect of iron supplementation on physical growth in children: systematic review of randomised controlled trials. *Public Health Nutr* 2006; **9**(7):904-20.

Salone, L., W. Vann and D. Dee. Breastfeeding: an overview of oral and general health benefits.*The Journal of the American Dental Association* 2013;**144**(2): 143-151.

Sampson HA, James JM, Bernhisel-Broadbent J, Yang E, Scanlon SM. Safety of an amino-acid derived infant formula in children allergic to cow milk. *Peditarics* 1992; **90**: 463-464.

Sandström B. Micronutrient interactions: effects on absorption and bioavailability. *British Journal of Nutrition* 2001 May;**85**(S2):S181-5.

Sankar MJ, Sinha B, Chowdhury R, Bhandari N, Taneja S, Martines J, Bahl R. Optimal breastfeeding practices and infant and child mortality: a systematic review and meta-analysis. *Acta Paediatr Suppl* 2015; **104** (467): 3-13.

Sassen ML, Brand R, Grote JJ. Breast-feeding and acute otitis media. *Am J Otolaryngol* 1994; **15**(5):351-7.

Savilahti E, Tainio VM, Salmenpera L, Siimes MA, Perheentupa J. Prolonged exclusive breastfeeding and heredity as determinants in infantile atopy. *Archives of Disease in Childhood* 1987; **62**: 269-73.

Savage JS, Fisher JO, and Birch LL. Parental Influence on Eating Behavior: Conception to Adolescence. *The Journal of Law Medicine & Ethics* 2007; **35**: 22–34.

Sayegh, A., E. Dini, R. Holt and R. Bedi. Oral health, sociodemographic factors, dietary and oral hygiene practices in Jordanian children. *Journal of dentistry* 2005; **33**(5): 379-388.

Scariati PD, Grummer-Strawn LM, Fein SB. A longitudinal analysis of infant morbidity and the extent of breastfeeding in the United States. *Pediatrics* 1997; **99**(6): E5.

Schaal B, Marlier L, Soussignan R. Human foetuses learn odours from their pregnant mother's diet. *Chemical Senses* 2000;**25**:729-737.

Schulz KF, Altman DG, Moher D, et al. CONSORT 2010 changes and testing blindness in RCTs. *Lancet* 2010; **375**: 1144–6.

Schwartz C, Issanchou S, Nicklaus S. Developmental changes in the acceptance of the five basic tastes by the first year of life. *Br J Nutrition* 2009;**102**:1375-1385.

Schwartz C, Scholtens PAMJ , Lalanne A, Weenen H, Nicklaus S. Development of healthy eating habits early in life, Review of recent evidence and selected guidelines. *Appetite* 2011; **57** (3): 796-807,

Schwartz C, Chabanet C, Laval C, Issanchou S, Nicklaus S. Breast-feeding duration: influence on taste acceptance over the first year of life. *Br J Nutrition* 2013;**109**: 1154-1161.

Scientific Advisory Committee on Nutrition (SACN), Subgroup on Maternal and Child Nutrition (SMCN). Paper for discussion: introduction of solid foods, agenda item: 3. 2003:(http://webarchive.nationalarchives.gov.uk/20140507012657/http://www.sacn.gov.uk/pdfs/smcn_03_08.pdf)

Scientific Advisory Committee on Nutrition (SACN). Salt and health. London:TSO; 2003.

Scientific Advisory Committee on Nutrition (SACN). Review of dietary advice on vitamin A. London:TSO; 2005.

Scientific Advisory Committee on Nutrition (SACN). Update on vitamin D: Position statement by the Scientific Advisory Committee on Nutrition. London: TSO; 2007.

Scientific Advisory Committee on Nutrition (SACN). Dietary Reference Values for Energy. London:TSO; 2011.

Scientific Advisory Committee on Nutrition (SACN). Iron and Health. 2010. London:TSO.

Scientific Advisory Committee on Nutrition (SACN). The influence of maternal, fetal and child nutrition on the development of chronic disease in later life. London: The Stationary Office; 2011.

Scientific Advisory Committee on Nutrition (SACN). Framework for the Ealution of Evidence. 2012 (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/480493/SACN_Framework_for_the_Evaluation_of_Evidence.pdf)

Scientific Advisory Committee on Nutrition Vitamin D and Health. The Stationery Office; 2016. (https://www.gov.uk/government/publications/sacn-vitamin-d-and-health-report)

Scientific Advisory Committee on Nutrition/Royal College of Paediatrics and Child Health. *Application of WHO growth standards in the UK*. London: The Stationary Office; 2007

SCF. Reports of the Scientific Committee for Food (Thirty-first series). Nutrient and Energy Intakes for the European Community; 1993.URL: http://ec.europa.eu/food/fs/sc/scf/out89.pdf

SCF. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Preformed Vitamin A (retinol and retinyl esters).P1-26; 2002.

Scoccianti C, Key TJ, Anderson AS, Armaroli P, Berrino F, Cecchini M, Boutron-Ruault MC, Leitzmann M, Norat T, Powers H, Schüz J, Wiseman M, Romieu I *et al*. European Code against Cancer 4th Edition: Breastfeeding and cancer. *Cancer Epidemiol* 2015; **39** (Suppl 1): S101-S106

Scott JA, Binns CW, Graham KI & Oddy WH. Predictors of the early introduction of solid foods in infants: results of a cohort study. *BMC Pediatrics* 2009; **9**: 60.

Scottish Dental Epidemiology Coordinating Committee. A report on the National Dental Inspection Programme of Scotland; 2016. (http://www.isdscotland.org/Health-Topics/Dental-Care/National-Dental-Inspection-Programme/.)

Seach KA, Dharmage SC, Lowe AJ & Dixon JB. Delayed introduction of solid feeding reduces child overweight and obesity at 10 years. *International Journal of Obesity (London)* 2010; **34**: 1475–9

Seely, E. W., E. M. Brown, D. M. DeMaggio, D. K. Weldon, and S. W. Graves. A prospective study of calciotropic hormones in pregnancy and post partum: reciprocal changes in serum intact parathyroid hormone and 1,25-dihydroxyvitamin D. *American Journal of Obstetrics and Gynecology* 1997;**176**(1 Pt 1): 214-7.

Selwitz, R., A. Ismail and N. Pitts. Dental caries. *The Lancet* 2007; **369**(9555): 51-59.

Shao J, Lou J, Rao R, Georgieff MK, Kaciroti N, Felt BT, Zhao ZY, Lozoff B. Maternal serum ferritin concentration is positively associated with newborn iron stores in women with low ferritin status in late pregnancy. *The Journal of nutrition* 2012;**142**(11):2004-9.

Sherriff A, Emond A, Hawkins N, Golding J, ALSPAC Children in Focus Study Team. Haemoglobin and ferritin concentrations in children aged 12 and 18 months. *Archives of Disease in Childhood* 1999;**80**(2):153-7.

Shukla A, Forsyth HA, Anderson CM, Marwah SM. Infantile overnutrition in the first year of life: a field study in Dudley, Worcestershire. *British Medical Journal* 1972; **4**: 507.

Siddappa AM, Georgieff MK, Wewerka S, Worwa C, Nelson CA, Deregnier RA. Iron deficiency alters auditory recognition memory in newborn infants of diabetic mothers. *Pediatric research* 2004;**55**(6):1034-41.

Singla PN, Tyagi M, Shankar R, Dash D, Kumar A. Fetal iron status in maternal anemia. *Acta Paediatrica* 1996;**85**(11):1327-30.

Simondon KB, Simondon F. Age at introduction of complementary food and physical growth from 2 to 9 months in rural Senegal. *European Journal of Clinical Nutrition* 1997; **51**: 703-7.

Silva DG, Franceschini SC, Sigulem DM. Growth in non-anemic infants supplemented with different prophylactic iron doses. *J Pediatr (Rio J)* 2008; **84**(4):365-372.

Skinner JD, Carruth BR, Bounds W, Ziegler P, Reidy K. Do food related experiences in the first 2 years of life predict dietary variety in school aged children *J Nutr Educ Behav* 2002; **34**(6): 310-5.

Small DM, Prescott J. Odor/taste integration and the perception of flavour. *Experimental Brain Research* 2005;**166**(3-4): 345-357.

Smith AM, Roux S, Naidoo NTR, Venter DJL. Food choices of tactile defensive children. *Nutrition* 2005; **21**: 14-19.

Smithers LG, Golley RK, Brazionis L and Lynch JW. Characterizing whole diets of young children from developed countries and the association between diet and health: a systematic review. *Nutr Rev* 2011; **69**: 449-67

Sowers, M., R. B. Wallace and J. H. Lemke. Correlates of forearm bone mass among women during maximal bone mineralization. *Preventive Medicine* 1985; **14**(5): 585-96.

Sowers, M. R., M. K. Clark, B. Hollis, R. B. Wallace and M. Jannausch. 1992. Radial bone mineral density in pre- and perimenopausal women: a prospective study of rates and risk factors for loss. Journal of Bone and Mineral Research 7(6): 647-57.

Specker, B. L., N. E. Vieira, K. O. O’Brien, M. L. Ho, J. E. Heubi, S. A. Abrams and A. L. Yergey. Calcium kinetics in lactating women with low and high calcium intakes. *American Journal of Clinical Nutrition* 1994; **59**(3): 593-9.

Stein LJ, Nagai H, Nakagawa M, Beauchamp GK. Effects of repeated exposure and health-related information on hedonic evaluation and acceptance of a bitter beverage. *Appetite* 2003; **40**:119-29.

Steinbrecher HA, Griffiths DM, Jackson AA. Urea production in normal breast-fed infants measured with primed/intermittent oral doses of [15N, 15N] urea. *Acta Paediatr* 1996; 85(6):656-62.

Steinkeller JS, Chan K, Rinehouse SE. Prechewing of food by adults and streptococcal pharyngitis in infants. *J Pediatr* 1992;**120**(4 pt 1): 563-4.

Sullivan SA, Birch LL. Infant dietary experience and acceptance of solid foods. *Pediatrics* 1994;**93**(2):271-7.

Sullivan PB. Cows’ milk induced intestinal bleeding in infancy. *Arch Dis Child*. 1993; **68**(2):240-245.

Sweet DG, Savage G, Tubman TR, Lappin TR, Halliday HL. Study of maternal influences on fetal iron status at term using cord blood transferrin receptors. *Archives of Disease in Childhood-Fetal and Neonatal Edition.* 2001;**84**(1):F40-3.

Taitz LS. Infantile overnutrition among artificially fed infants in the Sheffield Region. *British Medical Journal* 1971; **1**:315-316.

Taitz LS, Byers HD. High calorie/osmolar feeding and hypertonic dehydration. *Arch Dis Child* 1972; **47**:257-60.

Tamura T, Goldenberg RL, Hou J, Johnston KE, Cliver SP, Ramey SL, Nelson KG. Cord serum ferritin concentrations and mental and psychomotor development of children at five years of age. *The Journal of pediatrics* 2002;**140**(2):165-70.

Tham, R., G. Bowatte, S. Dharmage, D. Tan, M. Lau, X. Dai, K. Allen and C. Lodge. Breastfeeding and the risk of dental caries: a systematic review and meta-analysis.*Acta Paediatrica* 2015; **104**(S467): 62-84.

The Northern Ireland Statistics and Research Agency. Health Inequalities: Regional Report; 2016.

Thorsdottir IG, Atladottir BS. Palsson, G. Iron status at 12 months of age–effects of body size, growth and diet in a population with high birth weight. *Eur J Clin Nutr* 2003 ;**57**(4):505-13.

Thorisdottir AV, Thorsdottir I, Palsson GI. Nutrition and iron status of 1-year olds following a revision in infant dietary recommendations. *Anemia* 2011; **2011**.

Thorisdottir AV, Ramel A, Palsson GI, Tomassson H, Thorsdottir I. Iron status of one-year-olds and association with breast milk, cow's milk or formula in late infancy. *European journal of nutrition* 2013;**52**(6):1661.

Tilling K, Davies N, Windmeijer F, Kramer MS, Bogdanovich N, Matush L, Patel R, Smith GD, Ben-Shlomo Y, Martin RM, PROBIT Study Group. Is infant weight associated with childhood blood pressure? Analysis of the Promotion of Breastfeeding Intervention Trial (PROBIT) cohort. *Int J Epidemiol* 2011; **40**: 1227-37

Toschke AM, Martin RM, von Kries R, Wells J, Smith GD, Ness AR. Infant feeding method and obesity: body mass index and dual-energy X-ray absorptiometry measurements at 9-10 y of age from the Avon Longitudinal Study of Parents and Children (ALSPAC). *American Journal of Clinical Nutrition* 2007; **85**: 1578-1585

Townsend E, Pitchford NJ. Baby knows best? The impact of weaning style on food preferences and body mass index in early childhood in a case – controlled sample. *BMJ* Open 2012; **2**.

Trotter, M. and B. B. Hixon. Sequential changes in weight, density, and percentage ash weight of human skeletons from an early fetal period through old age. *Anatomical Record* 1974; **179**(1): 1-18.

Uhari M, Mantysaari K, Niemela M. A meta-analytic review of the risk factors for acute otitis media. *Clin Inect Dis* 1996; **22**(6): 1079-83.

Uijterschout L, Vloemans J, Vos R, Teunisse PP, Hudig C, Bubbers S, Verbruggen S, Veldhorst M, de Leeuw T, van Goudoever JB, Brus F. Prevalence and risk factors of iron deficiency in healthy young children in the southwestern Netherlands. *Journal of pediatric gastroenterology and nutrition* 2014;**58**(2):193-8.

US Preventive Services Task Force. Routine iron supplementation during pregnancy. Policy Statement. J*AMA* 1993;**270**:2846-8.

Vail B, Prentice P, Dunger DB, Hughes IA, Acerini CL, Ong KK. Age at Weaning and Infant Growth: Primary Analysis and Systematic Review. *J Pediatrics* 2015; **167**(2):317-324.

van Rossem L, Kiefte-de Jong JC, Looman CW, Jaddoe VW, Hofman A, Hokken-Koelega AC, Mackenbach JP, Moll HA & Raat H (2013). Weight change before and after the introduction of solids: results from a longitudinal birth cohort. *British Journal of Nutrition* **109**: 370–5

Veena SR, Krishnaveni GV, Wills AK, Hill JC, Karat SC & Fall CHD. Glucose tolerance and insulin resistance in Indian children: relationship to infant feeding pattern. *Diabetologia* 2011; **54**: 2533-2537

Venter C, Hasan Arshad S, Grundy J, et al. Time trends in the prevalence of peanut allergy: three cohorts of children from the same geographical location in the UK. *Allergy* 2010; **65**(1): 103-8.

Ventura AK, Mennella JA . Innate and learned preferences for sweet taste during childhood. *Current Opinion in Clinical Nutrition and Metabolic Care* 2011;**14**:379-384.

Vernacchio L, Lesko SM, Vezina RM *et al*. Racial/ethnic disparities in the diagnosis of otitis media in infancy. *Int J Pediatr Otorhinolaryngol* 2004;**68**(6):795-804.

Victora CG, Barros F, Lima RC, Horta BL, Wells J. Anthropometry and body composition of 18 year old men according to duration of breast feeding: birth cohort study from Brazil. *BMJ* 2003; **327**: 901

Walser M, Bodenlos LJ. Urea metabolism in man. *J Clin Invest*. 1959 ;**38**:1617-26.

Wardle J, Herrera ML, Cooke L, Gibson EL. Modifying children's food preferences: the effects of exposure and reward on acceptance of an unfamiliar vegetable. *Eur J Clin Nutr* 2003;**57**: 341-8.

Warren JJ, Weber-Gasparoni K, Marshall TA, Drake DR, Dehkordi-Vakil F, Dawson DV, Tharp KM. A longitudinal study of dental caries risk among very young low SES children. *Community Dentistry & Oral Epidemiology* 2009; **37**: 116-122.

Waterlow JC. The mysteries of nitrogen balance. *Nutr Res Rev.* 1999;**12**(1):25-54.

Weber M, Grote V, Closa-Monasterolo R, Escribano J, Langhendries J, Dain E, Giovannini M, Verduci E, Gruszfeld D, Socha P, Koletzko B. The European Childhood Obesity Trial Study Group. Lower protein content in infant formula reduces BMI and obesity risk at school age: follow-up of a randomized trial *Am J Clin Nutr* 2014 ; **99**(5):1041-1051.

Wells JCK, Jonsdottir OH, Hibberd PL, Fewtrell MS, Thorsdottir I, Eaton S, Lucas A, Gunnlaugsson G, Kleinman RE. Randomized controlled trial of 4 compared with 6 mo of exclusive breastfeeding in Iceland: differences in breast-milk intake by stable-isotope probe. *Am J Clin Nutr* 2012; **96**: 73-9.

Wells JC, Hallal PC, Wright A, Singhal A, Victora CG. Fetal, infant and childhood growth: relationships with body composition in Brazilian boys aged 9 years. *International Journal of Obesity* (London) 2005;**29**:1192-1198.

Whitaker RC, Pepe MS, Wright JA, Seidel KD, Dietz WH. Early adiposity rebound and the risk of adult obesity. *Pediatrics* 1998;**101**: e5

Wijnhoven TMA, de Onis M, Onyango AW, Wang T, Bjoerneboe GEA, Bhandari N, Lartey A, Rashidi BA. Assessment of gross motor development in the WHO Multicentre Growth Reference Study *Food and Nutrition Bullentin* 2004; **25** S37-45.

Wilkinson PW, Noble TC, Gray G, Spence O. Inaccuracies in measurement of dried milk powders. *British Medical Journal* 1973; **2**: 15-17.

Wilson AC, Forsyth JS, Greene SA, Irvine L, Hau C, Howie PW. Relation of infant diet to childhood health: seven year follow up of cohort of children in Dundee infant feeding study. *BMJ* 1998; **316**: 21-25.

Woo JG, Guerrero ML, Ruiz-Palacios GM, Peng Y, Herbers PM, Yao W, Ortega H, Davidson BS, McMahon RJ. Specific infant feeding practices do not consistently explain variation in anthropometry at age 1 year in urban United States, Mexico, and China Cohorts. *Journal of Nutrition* 2013;**143**: 166–174

Woolridge MW, Ingram JC, Baum JD. Do changes in breast usage alter the baby's nutrient intake? *Lancet* 1990; **336**(8712): 395-7.

World Cancer Research Fund / American Institute for Cancer Research, Continuous Update Project Report. Food, Nutrition, Physical Activity, and the Prevention of Breast Cancer; 2010. (http://www.dietandcancerreport.org/cup/cup_resources.php)

World Cancer Research Fund / American Institute for Cancer Research (2014) Continuous Update Project Report. Food, Nutrition, Physical Activity, and the Prevention of Ovarian Cancer; 2014. (http://www.dietandcancerreport.org/cup/cup_resources.php.)

World Health Organization. The optimal duration of exclusive breastfeeding. Report of an Expert Consultation. Geneva, Switzerland: World Health Organization; 2001.

World Health Organization. Global Strategy on Infant and Young Child Feeding. Geneva: WHO; 2003.

World Health Organization Working Group on Infant Growth. An evaluation of infant growth: document WHO/NUT/94.8. Geneva: WHO; 1994.

World Health Organization Multicentre Growth Reference Study Group (WHO MGRS). WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization; 2006a.

World Health Organization Multicentre Growth Reference Study Group (WHO MGRS). Enrolment and baseline characteristics in the WHO Multicentre Growth Reference Study. *Acta Pediatrica Suppl* 2006b 450:7-15.

World Health Organization/UNICEF. Joint Statement: Iron supplementation of young children in regions where malaria transmission is intense and infectious disease highly prevalent; 2006. (http://www.who.int/nutrition/publications/WHOStatement-_%20iron%20suppl.pdf)

World Health Organization. Department of Making Pregnancy Safer. WHO recommendations for the prevention of postpartum haemorrhage. Geneva: WHO; 2007.

World Health Organization/UNICEF. Complementary feeding of young children in developing countries: a review of current scientific knowledge. Geneva, World Health Organization; 1998 (WHO/NUT/98.1).

World Health Organization. Global strategy for infant and young child feeding. Geneva, Switzerland: World Health Organization; 2003.

World Health Organization. Infant and young child feeding. Model chapter for textbooks for medical students and allied health professionals. Geneva, World Health Organization; 2009.

World Health Organization & Centers for Disease Control and Prevention. Assessing the iron status of populations : including literature reviews : report of a Joint World Health Organization/Centers for Disease Control and Prevention Technical Consultation on the Assessment of Iron Status at the Population Level, 2nd ed. Geneva,Switzerland. 2004; http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/9789241596107.pdf

World Health Organization/ UNICEF. Meeting on infant and young child feeding. Geneva: WHO; 1979.

World Health Organization. Essential Nutrition Actions: Improving maternal newborn infant and young child health and nutrition. Geneva: WHO; 2013.

World Health Organization, UNICEF, USAID, AED, UCDAVIS, IFPRI. Indicators for assessing infant and young child feeding practices. Part I Definitions. Conclusions of a consensus meeting held 6–8 November 2007 in Washington D.C., USA. Geneva: WHO; 2008.

World Health Organization, UNICEF, USAID, AED, UCDAVIS, IFPRI. Indicators for assessing infant and young child feeding practices. Part II Measurement. Geneva: WHO; 2010.

World Health Organization. Requirements of vitamin A, thiamine, riboflavin and niacin. Report of a Joint FAO/WHO Expert Group; Rome, Italy. WHO Technical Report Series No. 362. WHO: Geneva; 1967

Wright CM, Parkinson KN, Drewett RF. Why are babies weaned early? Data from a prospective population based cohort study. *Arch Dis Child* 2004 **89**(9):813-6.

Wright CM1, Cameron K, Tsiaka M, Parkinson KN. Is baby-led weaning feasible? When do babies first reach out for and eat finger foods? *Maternal & Child Nutrition* 2011;**7**(1):27-33.

Wright CM, Cox KM, Sherriff A, Franco-Villoria M, Pearce MS, Adamson AJ. To what extent to weight gain and eating avidity during infancy predict later adiposity? *Public Health Nutrition* 2012; **15**:656-662.

Yang Z, Lönnerdal B, Adu-Afarwuah S, Brown KH, Chaparro CM, Cohen RJ, Domellöf M, Hernell O, Lartey A, Dewey KG. Prevalence and predictors of iron deficiency in fully breastfed infants at 6 mo of age: comparison of data from 6 studies. *Am J Clin Nutr*. 2009 May;**89**(5):1433-40.

Yuan W, Basso O, Sorensen HT, Olsen J. Maternal prenatal lifestyle factors and infectious disease in early childhood: a follow-up study of hospitalization within a Danish birth cohort. *Pediatrics* 2001;**107**: 357-362.

Zavaleta N, Lanata C, Burton B, Peerson JM, Brown KH, Lonnerdal B. Effect of acute maternal infection on quantity and composition of breast milk. *Am J Clin Nutr* 1995; **62**(3): 559-563.

Ziegler EE, Nelson SE, Jeter JM. Iron supplementation of breastfed infants from an early age. *Am J Clin Nutr* 2009; **89**: 525-32.

Ziegler EE, Fomon SJ, Nelson Se, Rebouche CJ, Edwards BB, Rogers RR, Lehman LJ. Cow milk feeding in infancy: further observations on blood loss from the gastrointestinal tract. *J Pediatr.* 1990; **116**(1): 1-18.

Zive MM, McKay H, Frank-Spohrer GC, Broyles SL, Nelson JA & Nader PR. Infant-feeding practices and adiposity in 4-y-old Anglo- and Mexican-Americans. *American Journal of Clinical Nutrition* 1992; **55**: 1104-8

Zivkovic AM, German JB, Lebrilla CB, Mills DA. Human milk glycobiome and its impact on the infant gastrointestinal microbiota. *Proceedings of the National Academy of Sciences of the United States of America* 2011; **108**: 4653-4658.

Zlotkin SH. Another look at cow milk in the second 6 months of life. *J Pediatr Gastroenterol Nutr.* 1993; **16**(1):1-3

Zhou SJ, Gibson RA, Gibson RS, Makrides M. Nutrient intakes and status of preschool children in Adelaide, South Australia*. Med J Aust,* 2012;**196**(11):696-700.