# NICE Maternal and Child Nutrition programme


# Review 5: The effectiveness of public health interventions to improve the nutrition of young children aged 6-24 months


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A review prepared for NICE by:

The Mother and Infant Research Unit
Department of Health Sciences
University of York
York, UK
YO10 5DD


Principal authors: Felicia McCormick, Jennifer A Moreton


Felicia McCormick
Jennifer A Moreton
Lalitha D'Souza
Sarah E King
Alison McFadden
Mary J Renfrew

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# 1   Executive Summary

This rapid review examines the effectiveness of public health interventions intended to promote safe and healthy feeding practices for infants and young children who are no longer predominantly milk fed.  Five key questions were addressed:

- What interventions effectively promote the timely introduction of appropriate supplementary feeds/solids, and/or family foods?
- What interventions effectively promote uptake of recommended vitamin and micronutrient supplements?
- What dietary strategies effectively reduce the risk of food allergies and intolerance?
- What dietary interventions help prevent diet-related dental caries, tooth loss and dental erosion in infants and young children?
- What interventions effectively help mothers continue breastfeeding after 6 months, both at home and out of home? (eg. to return to paid employment)

The search strategy was conducted in April 2006 using a stepped approach.  Initially, a worldwide search was conducted to identify relevant systematic reviews (from 1995 onwards) followed by randomised controlled trials (from 1990 onwards) and other study types (conducted in the UK and published from 1990 onwards).

A total of 9544 titles and abstracts were independently screened by two reviewers, and full paper copies of 63 systematic reviews, 79 randomised controlled trials and 25 UK studies were also independently assessed by two reviewers.  Five systematic reviews and seven randomised controlled trials (reported in fifteen papers) were data extracted and quality assessed by one reviewer and checked by a second reviewer.  There were a total of ten corraborative UK studies included in the review.

Two systematic reviews addressed effective promotion of timely introduction of appropriate solid/family foods.  Elkan et al. (2000) (2+) evaluated evidence from three randomised controlled trials and one non- randomised controlled trial and concluded that there was insufficient evidence to assess the effectiveness of home visiting on children's diets since the studies used maternal self-report to assess diet.  The two smaller trials were of disadvantaged families and the interventions gave significant dietary improvements.  One of these smaller studies was of sufficient quality (Gutelius et al. 1977).  Intensive home visiting by a health professional significantly improved daily milk intake, self-feeding, fruit or fruit juice and meat intake in children under 3 years whose mothers were unmarried, low-income, black schoolgirls (15-18 years).

Tedstone et al. (1998) (2++) evaluated evidence from five RCTs and one non-RCT and found that there was insufficient evidence to make recommendations about optimum weaning and post-weaning dietary practices.  At least four of these studies examined disadvantaged families.  However, three studies in the SR had positive outcomes.  A non-RCT within this SR (graded 'moderate' by the reviewers) found monthly visits by 'community mothers' significantly improved dietary intake of animal protein, non-animal protein, whole foods, milk, fruit and vegetables in infants under one-year of age from low-income families in Dublin (Johnson et al. 1993).  A large Finnish RCT (Lapinleimu et al. 1995, Niinikoski et al. 1996) (graded 'moderate/good' by the reviewers) found specific dietary counselling and health education conducted

in a health clinic reduced serum lipids and cholesterol levels in both boys and girls up to the age 36 months (significant only for boys) and was successful in reducing dietary intake of fat, saturated fat and cholesterol in both girls and boys up to age 36 months.  However, the nutritional aims of this study were beyond those currently considered necessary in the UK.  A US RCT in the SR (Frank et al. 1997) (graded 'good' by the reviewers) in predominately non-white low-income mothers during their post partum hospital stay and with two separate interventions found both research counselling and a research discharge pack delayed the introduction of solid foods.

No studies specifically addressing the key question of what interventions effectively promote uptake of recommended vitamin and micronutrient supplements were identified. Three studies within the Tedstone et al. SR (2++) (two RCTs (Childs et al. 1997, McEnery and Rao 1986) and one non-randomised controlled trial (Griffiths et al. 1995), all graded 'moderate' by the reviewers) evaluated three different interventions including home visiting by health visitors and health education for predominantly Asian low-income families living in the UK. All three interventions had no significant effect on the incidence of anaemia in children less than 18 months of age.  It is not clear whether all three study interventions promoted the uptake of recommended vitamin and micronutrient 'supplements' but two studies focussed on improving intakes of iron-rich foods and vitamin C (Childs et al. 1997, Griffiths et al. 1995). The RCT by McEnery and Rao (1986) had a wider focus which included 'child-rearing issues' but did compare vitamin supplement intake after the intervention but the result was not significant. Two studies were relatively small and had insufficient power (McEnery and Rao 1986, Griffiths et al. 1995).

A SR (2++) by Osborn and Sinn (2006) assessed the use of formula containing hydrolysed protein for prevention of allergy and food intolerance in infants and included eighteen studies. Interventions included the use of hydrolysed infant formulas including hydrolysed cow's milk and soy formulas, and extensively and partially hydrolysed formulas. Hydrolysed formulas could be used for: 1) early short term supplementary feeds or sole formula feeding in infants unable to be breastfed in the 1st few days; or 2) for prolonged supplementation or sole formula feeding in the first months. There were just two studies of short term feeding of hydrolysed formula in low risk infants which found no significant difference for any childhood allergy when compared to exclusive human milk or cow's milk formula but a higher incidence of infant cow's milk allergy with cow's milk formula (Saarinen 1999) than with hydrolysed formula or exclusive human milk. The authors concluded that "There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy compared to exclusive breastfeeding".

A meta-analysis of seven studies comparing prolonged feeding (for the first few months) of hydrolysed formula versus cow's milk formula in high risk infants gave a significant reduction for incidence of any infant allergy, RR 0.79, 95%CI: 0.66, 0.94 (De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993), but meta-analyses for incidence of individual allergies gave no significant difference for childhood allergy, infant asthma, infant eczema or childhood eczema. One study gave a significant reduction for infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89 (Vandenplas 1992). The authors of the review concluded that "In high risk infants who are unable to be completely breastfed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula reduces infant and childhood allergy and infant cow's milk allergy." The SR gave 2++ evidence for a reduction in incidence of any infant allergy associated with feeding hydrolysed formula for the first few months versus cow's milk formula.

Four studies in the SR (2++) by Osborn and Sinn (2006) compared prolonged feeding of extensively hydrolysed formula versus cow's milk formula (Mallet 1992, Oldaeus 1997, Szajewska 2001, Von Berg 2003) for which meta-analyses gave no significant difference for incidence of any infant allergy (two studies) or infant eczema (three studies). Meta-analysis for three studies (Mallet 1992, Oldaeus 1997, Von Berg 2003) gave a significant reduction in infant eczema incidence, RR 0.69, 95%CI: 0.47, 1.00, but the study by Von Berg et al (2003) contributed 75% weight to the meta-analysis. Von Berg et al (2003) also found a reduction in incidence of any childhood allergy, RR 0.72, 95%CI: 0.53, 0.97; infant eczema, RR 0.69, 95%CI: 0.47, 1.00; childhood eczema, RR 0.66, 95%CI: 0.44, 0.98; and prevalence of childhood eczema, RR 0.50, 95%CI: 0.27, 0.92.

Nine studies compared prolonged feeding of partially hydrolysed formula versus cow's milk formula for which meta-analyses gave no significant differences for incidence of childhood allergy, infant asthma, infant eczema, childhood eczema or infant rhinitis. Meta-analysis of seven studies found a significant reduction for any infant allergy, RR 0.79, 95%CI: 0.65, 0.97 (De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993). One study found a significant reduction in infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89 (Vandenplas 1992). One of the nine studies was of partially hydrolysed casein containing formula and reported no significant differences for incidence of any allergy (Oldaeus 1997). The remaining eight studies compared prolonged feeding of partially hydrolysed whey formula versus cow's milk formula for which the overall conclusions for partially hydrolysed formula are unchanged. The SR therefore gave 2++ evidence for a reduction in incidence of any infant allergy associated with feeding partially hydrolysed formula (in particular partially hydrolysed whey formula) for the first few months versus cow's milk formula.

The SR (2++) by Osborn and Sinn (2006) contained four studies that compared prolonged feeding of extensively hydrolysed formula versus partially hydrolysed formula (Halken 2000, Nentwich 2001, Oldaeus 1997, Von Berg 2003). No significant differences were found for any individual study or for meta-analyses of incidence of any infant allergy, infant asthma or infant eczema. However, there was a significant reduction in incidence of infant food allergy (two studies), RR 0.43, 95%CI: 0.19, 0.99 (Halken 2000, Oldaeus 1997). The authors concluded that "In view of methodological concerns and inconsistency of findings, further large, well-designed trials comparing formulas containing partially hydrolysed whey, or extensively hydrolysed casein to cow's milk formula are needed.

Six randomised controlled trials evaluated strategies to reduce the risk of food allergies and intolerance. A single randomised controlled trial conducted in Finland (Kalliomaki et al., 2001, 2003) provided 1+ evidence that probiotic Lactobacillus GG given to the infant or breastfeeding mother during the first 6 months of life is likely to be effective at reducing atopic eczema in children at risk of developing atopic disease. One UK randomised controlled trial (Arshad et al. 1992, Hide et al. 1994, 1996) provided 1+ evidence that reduced exposure to allergenic foods and house-dust mites in the first year of life effectively reduces the prevalence of asthma and eczema at 12 months in children with a family history of atopy. This intervention remained effective at ages two and four years, with the exception of asthma. A Dutch randomised controlled trial (Schonberger et al. 2005) similarly used a multifaceted educational preventive strategy to reduce exposure to mite, pet and food allergens and passive smoking in high risk children in the first two years of life. This RCT provides 1++ evidence that the intervention was not effective in reducing asthma-like symptoms during the first two years but was modestly effective at age 2 years. However, there were significant outcomes for girls but not for boys during the

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first two years. Breastfeeding was significantly negatively correlated with wheezing at age two years or earlier. Three randomised controlled trials examined the effectiveness of modified cow's milk formulae *and* dietary restriction to prevent atopy in children at high risk. One (1-) trial conducted in Sweden and Finland (Odelram et al. 1996) found no significant differences between children given ultra-filtered cow's milk whey formula and those given standard cow's milk formula. Another study (1-) conducted in Sweden (Oldaeus et al. 1997) reported more positive outcomes in breastfed children given an extensively hydrolysed casein formula in comparison to a partially hydrolysed formula, or a routine cow's milk formula on weaning. The socio-economic status of participants in these Swedish studies was not reported. Similarly, a German study (Von Berg et al. 2003) (1-) also reported more positive outcomes among children receiving an extensively hydrolysed casein formula compared to conventional cow's milk formula, however partially and extensively hydrolysed whey formulae were not effective (see above). A glossary of terms used in these five randomised controlled trials appears at the end of this Executive summary.

Two studies relevant to dental health promotion in this age group were included. These were an English language summary (2-) of a Swedish systematic review (Holm et al. 2002), but this identified no studies that examined the effect of dietary information on preventing caries in this age group, and insufficient information on whether sugar substitutes have any preventive effects on caries, and a recently published UK guideline (SIGN 2005) (2+) that used systematic review methodology. The SIGN review included two studies which applied to children aged 6-24 months. The first was a systematic review by Valaitis et al. (2000) (graded 2+ by the SIGN reviewer). This review found no consistent high quality evidence for an association between breastfeeding beyond one year and the development of early dental caries. The second was a systematic review by Reisine & Psoter (2001) (graded 2+ by the SIGN reviewer). This review was based on poor quality studies and found evidence that the duration of bottle use was not related to caries risk but weak evidence that sweetened milk or juice in a bottle increased the risk of early childhood caries (at age <6 years).

One pilot study was identified that specifically aimed to support breastfeeding after six months in women who planned to return to work (Jones et al. 2004). This study was given a minus rating and no evidence statement was derived from this work.

Weaning is an important time in the life of a family, when healthier eating patterns can be established. Overall, this rapid review identifies important gaps in the evidence base. No studies have been found that address the practical problems of weaning (such as choosing and preparing appropriate foods, behavioural problems in the child such as food refusal, tiredness in the mother). There is a paucity of information on follow-on formula milks, which are widely available and widely used, and on the use of bottles/cups/spoons as ways of feeding fluids to older babies. No evaluations of strategies either to assist mothers to wean successfully or to encourage children and families to eat a wide range of healthy foods, and resist unhealthy foods, have been identified. These issues need to be further explored to inform recommendations about weaning.

## 1.1 References to included papers, and methodology checklist ratings

### 1.1.1 Systematic reviews including an assessment of interventions to improve children's diets

| Reference | Methodology checklist rating |
|---|---|
| Elkan R, Kendrick D, Hewitt M, et al. (2000) The effectiveness of domiciliary health visiting: a systematic review of international studies and a selective review of the British literature. Health Technology Assessment. **4** (13):1-339. | 2+ |
| Tedstone A, Dunce N, Aviles M, Shetty PS. (1998) Effectiveness of interventions to promote healthy feeding in infants under one year of age. London: Health Education Authority. | 2++ |

### 1.1.2 Systematic reviews including an assessment of interventions to promote uptake of recommended vitamin and micronutrient supplements

| Reference | Methodology checklist rating |
|---|---|
| Tedstone A, Dunce N, Aviles M, Shetty PS. (1998) Effectiveness of interventions to promote healthy feeding in infants under one year of age. London: Health Education Authority. | 2++ |

### 1.1.3 Studies evaluating baby milk formula, allergenic foods or probiotic interventions to reduce the risk of food allergies and intolerance

| Reference | Methodology checklist rating |
|---|---|
| Osborn DA & Sinn J. (2006) Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants. Cochrane Database of Systematic Reviews 2006, Issue 4. Art.No.:CD003664. DOI: 10.1002/14651858.CD003664.pub3. | 2++ |
| Arshad SH, Matthews S, Gant C, et al. (1992) Effect of allergen avoidance on development of allergic disorders in infancy. Lancet. **339** (8808):1493-7. Hide DW, Matthews S, Matthews L, et al. (1994) Effect of allergen avoidance in infancy on allergic manifestations at age two years. Journal of Allergy & Clinical Immunology. **93** (5):842-846. Hide DW, Matthews S, Tariq S, Arshad SH (1996) Allergen avoidance in infancy and allergy at 4 years of age. Allergy. **51**(2): 89-93. | 1+ |
| Kalliomaki M, Salminen S, Arvilommi H et al. (2001) Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. Lancet. **357** (9):9262. Kalliomaki M, Salminen S, Poussa T, et al. (2003) Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. Lancet. **361** (9372):1869-71. | 1+ |
| Odelram H, Vanto T, Jacobsen L, et al. (1996) Whey hydrolysate compared with cow's milk-based formula for weaning at about 6 months of age in high allergy-risk infants: effects on atopic disease | 1- |

| | |
|---|---|
| and sensitization. Allergy. **51** (3):192-5. | |
| Oldaeus G, Anjou K, Bjorksten B, et al. (1997) Extensively and partially hydrolysed infant formulas for allergy prophylaxis. Archives of Disease in Childhood. **77** (1):4-10. | 1- |
| Schonberger HJAM, Dompeling E, et al. (2005) The PreVASC study: the clinical effect of a mulifaceted educational intervention to prevent childhood asthma. European Respiratory Journal. **25**: 660-670. | 1+ |
| Von Berg A, Koletzko S, Grubl A, et al. (2003) The effect of hydrolyzed cow's milk formula for allergy prevention in the first year of life: The German Infant Nutritional Intervention Study, a randomized double-blind trial. Journal of Allergy & Clinical Immunology. **111** (3):533-540. | 1- |

### 1.1.4 Systematic reviews of studies of dental health promotion

| Reference | Methodology checklist rating |
|---|---|
| Holm AK, Axelsson S, Dahlgren H, et al. (2002) Prevention of dental caries. Stockholm: Swedish Council on Technology Assessment in Health Care (SBU). | 2- |
| SIGN. (2005) Prevention and management of dental decay in the pre-school child. In: Guideline no.83: SIGN. Scottish Intercollegiate Guidelines Network, NHS Scotland. | 2+ |

### 1.1.5 Randomised controlled trials of interventions to support continued breastfeeding beyond 6 months

| Reference | Methodology checklist rating |
|---|---|
| Jones E. (2004) Breastfeeding and returning to work. Practising Midwife. **7** (11):17-18, 20, 22. | 1- |

## 1.2 Glossary

### 1.2.1 Allergy terms used in RCTs

IgE — Immunoglobulin E. IgE antibodies play a key role in very early recognition of foreign material ('gatekeeper function'). The reaction triggered by IgE may be considered beneficial to the host as typically it expels allergenic proteins from the body.

Allergic rhinitis — A symptomatic disorder of the nose caused by immunoglobulin E – mediated (IgE-mediated) inflammation after the membranes of the nose have been exposed to allergens. Originally classified as seasonal, perennial or occupational but recently reclassified as mild intermittent, mild persistent, moderate-severe intermittent or moderate-severe persistent. Seasonal allergic rhinitis is commonly called hay fever.

Asthma — A chronic respiratory disease, often arising from allergies, characterised by sudden recurring attacks of laboured breathing, chest constriction and coughing.

Dermatitis — Inflammation of the skin

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|---|---|
| Eczema | A general term for the several types of inflammation of the skin. |
| Atopic dermatitis | The most common of the many types of eczema. A chronic disease affecting the skin where the skin becomes extremely itchy. Scratching leads to redness, swelling, cracking, 'weeping' clear fluid, and, finally, crusting and scaling. |
| Urticaria | An allergic skin condition also called hives or nettle-rash or wheals, simply means itching with a rash. Medically defined as a skin eruption, which is allergic in origin and characterised by profound itching with red circular or irregularly shaped eruptions on any part of the body. |
| Atopic diseases | A group of diseases where there is often an inherited tendency to develop more than one other allergic conditions. |
| Probiotic | The use of micro-organisms in a positive way to benefit health. Probiotics are usually consumed in specially designed foods that are variously called functional foods, nutraceuticals or FoSHUs (foods for specified health uses). |
| Colony-forming units | Colonies are collections of bacterial cells visible to the naked eye resulting from growth on agar gels. It is generally assumed that one bacterial cell will, after numerous cell divisions, eventually form a colony but a 'colony-forming unit' might be 1 or >1 live bacterial cells. |

### 1.2.2 Infant formula terms used in RCTs

Information chiefly from the body representing the UK manufacturers of specialist nutrition products – the Infant and Dietetic Food Association (IDFA) website (www.idfa.org.uk/) with further details from included papers. Each infant formula variety or brand will differ even if they fit into the same broad category.

| | |
|---|---|
| Regular cow's milk formula | Infant formula 'based on cow's milk, with the protein altered to make it suitable for babies.' |
| Casein | The major and largest protein present in milk. |
| Whey-based formula | The cow's milk protein is adjusted so that the casein: whey ratio is similar to that in breast milk (40:60). (NB *Beba HA* was 100% whey) Whey-based milks may also have a lower mineral content (in particular sodium and potassium). |
| Casein-based formula | Contains more casein than whey. The casein: whey ratio is similar to that in cow's milk (80:20). (NB *Hipp HA* formula was 100% casein.) |
| Protein hydrolysate | Product of protein hydrolysis. |
| Hydrolysed infant formula | Milk proteins enzymatically digested to produce smaller protein molecules (peptides). |

| Partially hydrolysed infant formula | Milk proteins only partially enzymatically digested. (NB % peptides >6000 d in *Beba HA* was 18%.) |
|---|---|
| Extensively hydrolysed infant formula | Milk proteins extensively enzymatically digested. (NB % peptides >6000 d in *Nutramigen* and *Hipp HA* were 0.5% and 2%, respectively.) |
| Hydrolysed ultra filtered cow's milk whey formula | Whey proteins enzymatically digested to produce smaller peptides, then ultra filtered to select peptide size. |
| Soya-based formula | Nutritionally similar to cow's milk-based formulas but the protein is from soya and the lactose replaced by permitted carbohydrates (glucose syrups). 'Suitable for infants who cannot tolerate cow's milk either due to an allergy to cow's milk protein and/or due to an inability to digest the lactose in cow's milk.' They should only be given on medical advice and are not the first choice for infants with allergy to cow's milk protein, lactose intolerance, galactokinase deficiency or galactosaemia. |

## 2 Evidence statements

1. There is evidence from one RCT (Gutelius et al. 1977 graded moderate quality by reviewer) reported in a systematic review (Elkan et al. 2000 2+) that intensive home visiting by a health professional significantly improved daily milk intake, self-feeding, fruit or fruit juice and meat intake in children under 3 years whose mothers were unmarried, low-income, black school girls (15-18 years).

2. One study (Johnson et al. 1993 non-RCT graded moderate quality by reviewer) included in the Tedstone systematic review (Tedstone et al. 1998 2++) found monthly visits by 'community mothers' significantly improved dietary intake of animal protein, non-animal protein, whole foods, milk, fruit and vegetables in infants under one-year of age from low-income families in Dublin.

3. A large RCT (Lapinleimu et al. 1995; Niinikoski et al. 1996 graded moderate quality by reviewer) in the Tedstone systematic review (Tedstone et al. 1998 2++) found specific dietary counselling and health education conducted in a health clinic reduced serum lipids and cholesterol levels in both boys and girls up to the age 36 months (significant only for boys) and was successful in reducing dietary intake of fat, saturated fat and cholesterol in both girls and boys up to age 36 months.

4. A US RCT (Frank et al. 1995 graded good quality by reviewer) in the Tedstone systematic review (Tedstone et al. 1998 2++) in predominately non-white and low-income mothers during their post partum hospital stay and with two separate interventions found both research counselling (p=0.03) and a research discharge pack (p=0.02) delayed the introduction of solid foods by 14 and 8 days, respectively.

5.  Two RCTs (Childs et al. 1997 graded moderate quality by reviewer and McEnery and Rau 1986 graded poor quality by reviewer) and one non-RT (Griffiths 1995 graded moderate quality by reviewer) in the Tedstone systematic review (Tedstone et al. 1998 2++) evaluated three different interventions including home visiting by health visitors and health education in children under 18 months of age from predominantly Asian low-income families living in the UK. There was no effect on the incidence of anaemia.

6.  A systematic review (Osborn and Sinn 2006 2++) of 13 RCTs and five quasi-randomised trials concluded that: There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy compared to exclusive breast feeding. In high risk infants who are unable to be completely breast fed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula reduces infant and childhood allergy and infant cow's milk allergy. In view of methodological concerns and inconsistency of findings, further large, well designed trials comparing formulas containing partially hydrolysed whey, or extensively hydrolysed casein to cow's milk formulas are needed.

7   A single RCT (Kalliomaki et al. 2001; 2003 1+) examined the effect of giving Lactobacillus GG to breastfeeding mothers from atopic families or their infants. Mothers received two capsules of $10^{10}$ Lactobacillus GG daily for two weeks prior to delivery and postnatally for six months. Infants were given the capsule contents diluted with water on a spoon.  The incidence of atopic eczema in children was significantly reduced up to 4 years of age, whether capsules were given to the breastfeeding mother or infant. There were no significant differences in other indicators of atopic disease.

8.  A single RCT in infants with a family history of atopy (Arshad et al. 1992; Hide et al. 1994; Hide et al. 1996 1+) showed that a package of interventions including reduced exposure to allergens in food for breastfeeding mothers and infants, and a reduced exposure to house dust, reduced the frequency of allergic disorders at twelve months. Parental smoking was a significant risk factor for total allergy at 12 months (p<0.05). Infants from low socio-economic groups had a higher risk of developing allergy than those from a higher socio-economic group (p<0.05).

Follow-up at ages 2 and 4 years showed that the infants in the control group remained more likely to develop any allergy (p<0.005 at age 2 years; p<0.02 at age 4 years) and eczema (p=0.008 at age 2 years; p<0.05 at age 4 years) but the enhanced risk of asthma was no longer significant.

9.  One under powered RCT (Oldaeus et al. 1997 1-) compared extensively hydrolysed casein formula, partially hydrolysed whey formula and infant formula from the start of weaning to age 9 months in infants with a family history of atopy. Allergy preventive measures were also recommended including discouraging smoking and dietary exclusion of cow's milk, eggs, fish and citrus fruits in both mothers and infants diets. The study found hydrolysed casein formula had a positive allergy-preventive effect during the first 18 months of life but not partially hydrolysed whey formula when compared to standard infant formula.

10.      A single RCT (Schonberger et al. 2005 1+) in infants at high risk of developing asthma used a multifaceted intervention in which families received instructions from nurses at 4-6 months pregnant, 8 months pregnant and 1-3 weeks after the birth on how to reduce exposure to mite, pet and food allergens, and passive smoking. The dietary recommendations were to breastfeed for ≥6 months and, if supplementation was necessary or if breastfeeding stopped before age 6 months, to use extensively hydrolysed formula milk and to postpone the introduction of solid foods until age 6 months.

During the first 2 years of life, the incidence of asthma-like symptoms was similar in both groups: however, subanalysis revealed a significant reduction in the female, but not the male intervention group. At age 2 years, the intervention group had fewer asthma symptoms, including wheezing, shortness of breath and night-time cough than the control group.

Feeding hypoallergenic formula or the introduction of solid foods at <6 months were not significantly associated with asthma symptoms at age 2 years or earlier but breastfeeding was significantly negatively correlated with wheezing at age 2 years or earlier.


11. A systematic review (Valaitis et al. 2000 graded 2 + by reviewer) of 28 articles of varying quality, reported in dental guidance/ systematic review by the Scottish Intercollegiate Guidelines Network (SIGN) (2005 2+) found no consistent high quality evidence of an association between breastfeeding beyond one year and the development of early dental caries.


12. A systematic review (Reisine and Psoter 2001, graded 2+ by reviewers) reported in dental guidance/systematic review by SIGN (2005 2+) based on poor quality studies found evidence that the duration of bottle use (specifically beyond age 12 months) was not related to caries risk but weak evidence that sweetened milk or juice in a bottle increased the risk of early childhood caries (at age <6 years).

# 3   Background

## 3.1   Current dietary recommendations for children of 6-24 months

The scientific basis of dietary recommendations for children aged from 6 months -24 months in the UK, are for the most part, based on the 1994 COMA report on, *'Weaning and the weaning diet'*, with some important subsequent updates.

The current recommendation from the Department of Health is that mothers should breastfeed exclusively for six months and to delay introduction of solid foods until six months of age.

Advice for the public on diet during the period from 6 to 24 months is provided by the Food Standards Agency through their website http://www.eatwell.gov.uk/agesandstages/baby/weaning/ and the Department of Health in  *'Birth to five'* which is available free of charge to all first time parents.

During this period, children continue with milk feeds. The Food Standard Agency reports that soya formula be given to babies only when advised by a GP or health visitor (for example, in cases were a baby can't or won't drink other types of formula or if non-breastfeeding parents want the baby to eat a vegan diet). Soya infant formula was originally developed for babies who couldn't have infant cows' milk, because of a milk allergy, for example. There are now other types of formula that are more suitable for these babies.

### 3.1.1   Feeding children from 6 -12 months

During the period 6 -12 months, most babies in the UK are in the process of being weaned.  The weaning process can be defined as the gradual transition from an exclusively milk based diet to a diet based, for the most part, on foods other than milk.

Key issues which arose from the COMA report on weaning and which advice to the public therefore reflects includes:

- The timing of the first introduction of any solid foods
- The timing of the introduction of particular foods/food groups, in order to reduce the risk of developing allergies
- Meeting the infants' nutritional needs through introducing a variety of foods
- Protecting oral health through choosing appropriate foods and drinks
- The use of vitamin supplements

### 3.1.2   Timing of the first introduction of any solid food

In 1994, COMA recommended that *'the majority of infants should not be given solid foods before the age of four months, and a mixed diet should be offered by the age of six months'.*  In 2001, the World Health Organisation recommended that mothers should breastfeed exclusively for 6 months and thereafter solid foods should be introduced while breastfeeding continues for up to 2 years and beyond. This recommendation was adopted by English Health Departments and advice to the public, which had previously recommended first introducing solid foods not before 4 months, but by 6 months (i.e. between 17-26 weeks), was therefore revised.  The new advice encouraged all mothers, whether they were breast or bottle feeding, to delay introducing solids until 6 months. In recognition that some infants are, in reality,

weaned earlier than this, advice to the public warned against introducing first solids before 4 months or 17 weeks.

### 3.1.3 Timing of the introduction of particular foods/ food groups to reduce the risk of allergy

In its' 1994 report, COMA recommended that in order to reduce the risk of developing allergies, weaning before 4 months should be discouraged and foods which are traditionally regarded as allergenic should not be introduced before 6 months. This is particularly the case where there is a family history of allergy.

Guidance for the public issued by the Department of Health and the Food Standards Agency therefore recommends that the following foods are avoided before 6 months, due to the risk of developing allergies:

- Cereals which contain gluten, including wheat, rye and barley
- Milk other than breast or formula milk
- Eggs
- Fish and shellfish
- Citrus fruits
- Nuts, including peanuts, and seeds

It is also advised that honey is not given to babies under the age of 1, because of the risk of infant botulism and that salt and sugar are not added to food for babies.

In the UK, the recommended first weaning foods are non-wheat based cereals such as rice, and vegetables and fruits (other than citrus fruit).  This is often referred to as 'stage 1' of weaning.  Advice for the public recommends that where possible, homemade foods are used in order that the baby gets used to the foods the family eats and is introduced to a wide range of flavours and textures.  Parents and carers are advised to introduce these first foods initially just once a day, starting with just a taste and gradually increasing the amount, and being led by the baby's appetite. At this stage, the main source of energy and nutrients remains the milk feeds, and it is recommended that the baby continues to receive at least 500-600mls/ day breast or formula milk.


### 3.1.4 Meeting nutritional needs and introducing a variety of foods

COMA stressed the importance of ensuring an adequate intake a range of nutrients, in particular iron beyond the first 6 months.  Weaning advice to the public therefore encourages the extension of the range of foods in the baby's diet, both in order to provide all the nutrients that the baby needs and to ensure they will ultimately eat a varied family diet.

Beyond six months the potentially allergenic foods listed above, with one or two exceptions can be gradually introduced and it is advised that they are introduced one at a time, so that if there is an allergic reaction, it is easy to identify which food may have been the cause.  The exceptions are as follows:

- Pasteurised cows' milk may be used for mixing foods or in cooking but is not suitable as a drink until the baby is one year old. Only full fat milk should be used. Semi skimmed milk should not be introduced until the age of 2 years and skimmed milk not introduced before the age of 5 years.

- Where there is a close family history of asthma, eczema, hay fever or other allergy, peanuts and peanut containing products should not be introduced before the age of 3 years and all whole nuts should be avoided until the child is 5 years old due to risk of choking.
- The Food Standard Agency also advises that parents may wish to avoid giving raw shellfish to babies and young children to reduce the risk of food poisoning.

During 'stage 2 weaning', it is therefore recommended that meat, poultry, fish and/or pulses be introduced and that full fat cows' milk products such as yoghurt and fromage frais, custards and cheese sauce can be introduced as can well-cooked eggs. The use of homemade foods is again encouraged. At the same time, parents and carers are encouraged to introduce 'solid' foods at two and then three meals a day, again gradually increasing the amount of food offered.

Between 6 and 9 months, solid foods should gradually become a larger part of the baby's diet. At around 9 months and 'stage 3' of weaning, it is recommended that foods are now mashed so that the baby learns to cope with lumps and starts to learn to chew even if their teeth haven't yet appeared. The introduction of finger foods is encouraged, (bread, toast, sticks of vegetables, cheese and peeled fruits). It is recommended that at this stage, the baby has 2-3 servings of starchy foods each day, fruit and vegetables at two or more meals each day and one serving of meat, poultry, fish, egg, pulses or tofu each day. The importance of red meat as a source of iron is emphasised and it is recommended that those babies who do not eat meat have a diet rich in vitamin C in order to enhance the absorption of non meat (non-haem) sources of iron. In particular it is recommended that foods or drinks rich in vitamin C are served at the same meal.

From about 9 months onwards, parents and carers are encouraged to move towards foods that are chopped or minced and increase the number of servings of foods from different food groups, so that by the time they are a year old, they are eating three main meals a day with snacks in between to ensure that energy and nutrient needs are met. This is sometimes called 'Stage 4' weaning and reflects the advice by COMA that *'by the age of one year the diet should be mixed and varied'.*

### 3.1.5   Protecting oral health through choosing appropriate foods and drinks

Advice to parents and carers throughout the weaning period reflects COMA's advice to choose foods and drinks low in non-milk extrinsic sugars in order to protect the baby's oral health. Parents and carers are advised not to add sugar to foods for babies, in order to avoid the development of sweet preferences – a higher initial exposure has been shown to affect later preference and consumption. Up until the age of one year, cooled boiled water is the preferred option for drinks in addition to breast milk or infant formula. It is recognised that giving fruit juice after six months may be useful as a method of enhancing the absorption of iron due to its vitamin C content, but this should be well diluted (1 part juice to 9 parts water), given at mealtimes only and from a cup as opposed to a bottle. Dilutable squashes, fizzy drinks and baby herbal drinks are not recommended.

One of the key areas for action in the 'Choosing Better Oral Health' White paper (Department of Health, 2005a) is to improve the diet and reduce sugar intake by:

- Reducing the frequency and amount of added sugars consumed in line with the Government's target of 11% of food energy.

- Increasing the consumption of fruit and vegetables to at least five portions a day and promoting the use of sugar free medicines.

COMA also advised that from six months infants should be introduced to drinking from a cup, rather than a bottle.

### 3.1.6 Use of supplements

From the age of six months COMA recommends the use of supplements of vitamins A and D for babies which are predominantly breastfed. This is not recommended for babies that are exclusively fed on infant formula as this product is fortified with these vitamins.

### 3.1.7 Key issues for children of 6-12 months

- The early introduction of any first solid foods particularly among lower income groups
- The early introduction of gluten and to some extent, cows milk products
- Encouraging the use of homemade foods, as opposed to commercially prepared foods particularly in the first stage of weaning
- Stressing the importance of sources of iron in the diet and ways of ensuring it is well absorbed from diets which do not contain meat
- Promoting the use of supplements of vitamins A and D among breast fed babies after 6 months of age

## 3.2 Feeding children from 12-24 months

By the time children have reached their first birthday, they should be eating a varied mixed diet. As this is a period of rapid growth and development, the needs for energy and nutrients are high and this is recognised by the advice which is given to the public in *'Feeding your toddler'*.

This stresses including:

- a variety of foods from each of the food groups every day to ensure that a range of nutrients are provided
- energy and nutrient dense foods, due to young children being unable to eat a large quantity of food at each meal. The importance of providing full fat dairy foods is stressed for this reason, as is the need to provide small nutritious frequent snacks in addition to main meals,
- full-fat cows milk as a main drink from a year old. Semi skimmed milk can be introduced from two years of age
- foods rich in iron each day for example meat, beans, dried fruit , whole grains fortified breakfast cereals, especially where meat is not given, and  giving vitamin C rich foods or diluted juice at mealtimes
- supplements of vitamins A, C, and D from the age of 1 until the age of 5

 And stresses avoiding

- sugary foods and drinks in order to protect oral health
- low fat and diet products and diets which are too high in fibre,
- adding salt to foods for children and giving salty snacks
- tea and coffee as this reduces iron absorption

- whole nuts until the age of five, because of the risk of choking and peanuts and peanut containing products until the age of three where there is a close family history of asthma, eczema, hay fever or other allergies
- some specific foods due to food safety considerations, in addition to general food safety and hygiene precautions, e.g. avoiding raw or undercooked eggs and raw shellfish, due to the risk of food poisoning and avoiding certain fish which may be high in mercury, such as swordfish, shark and marlin

The most recent national survey which looks at the diets of children in the age range 12-24 months is the National Diet and Nutrition Survey of children aged 1½ to 4½, which was published in 1995 (Gregory et al. 1995). The data is now a decade old and needs to be updated. However at the time, the following data relevant to the above recommendations was recorded.

Whole milk, white bread, and biscuits were the foods most commonly consumed by this age group, being eaten by over 80%. The variety of vegetables and fruit consumed appears to be limited, with carrots, peas and baked beans being the most popular vegetables and bananas, apples and pears being the most popular fruits, all consumed by around half of the children of this age.

Seventy four percent of children aged between 18 months and 2½ years were drinking full fat cows' milk as is recommended, 12% were having semi skimmed milk and 9 % did not have milk to drink. Thirty three percent were introduced to cows' milk at or after 12 months of age, with 27% being introduced to it earlier than recommended at between 6 and 9 months and a further 27% between 9 and 12 months.

Average daily intakes of iron were well below the reference nutrient intake for children of this age range and almost a quarter (24%) had intakes below the lower reference nutrient intake.  Haemoglobin concentrations of below 11.0g/dl were considered as being an indication of anaemia and one in eight children in this age range was considered to be so, using this definition. Only 5% children of all ages in the survey were taking iron supplements.  The main sources of iron in the diet were cereal products, including fortified breakfast cereals, vegetables, and meat and meat products. Over two-thirds of children of this age, were consuming tea which interferes with the absorption of iron.

Almost a fifth (19%) of children were taking supplements, with over two thirds of these being either multivitamins (without iron) (36%), or vitamins A, C, and D, (39%) (including those available under the former Welfare Food Scheme). However children from non-manual backgrounds were more likely to take them than those from manual backgrounds and those children who did take supplements tended to have higher intakes of these nutrients from the diet than those who did not.

Two-thirds of children in the survey were eating chips and almost three-quarters savoury snacks including crisps. Eighty percent were consuming non-diet soft drinks, and 41% diet drinks. Seventy percent were consuming chocolate and 46% sugar confectionery. On average around 17% energy was derived from non milk extrinsic sugars in children of this age group, compared to the COMA recommendation of a maximum of 10%.  Of these, around a third came from non-diet soft drinks, excluding fruit juice, a  fifth from cereal and cereal products, including biscuits and breakfast cereals and a quarter from sugar, confectionery and preserves.

### 3.2.1  Key issues for children of 1-2 years, appear therefore to include:

- increasing the variety of foods consumed, particularly fruits and vegetables
- the early introduction of cows' milk as drink
- low iron intakes and the rates of anaemia
- low uptake of vitamin D supplements, particularly among manual groups
- high intakes of non milk extrinsic sugars, particularly from soft drinks and confectionery.


## 3.3  Promoting a healthy diet for children of 6-24 months

The Governments' White Papers 'Choosing Health', 'Choosing a Healthy Diet' and 'Choosing Better Oral Health' outline plans to promote a healthy diet throughout peoples' lives (Department of Health 2005a, 2005b and 2005c). There are two key policy initiatives which are directed particularly at improving the diets of pregnant women and children under the age of five. These are Sure Start and 'Healthy Start'. Both of these will contribute towards the more integrated child health services outlined within the National Service Framework for Children, Young People and Maternity Services and the 'Every Child Matters: Change for Children Programme'.

The Government's Healthy Start has  replaced the former Welfare Food Scheme under which infant formula, liquid cows milk and vitamin drops of vitamins A, C, and D were available free to those who qualified for the scheme.  Healthy Start  makes fresh fruit and vegetables available to those who qualify in addition to cows' milk and infant formula through a voucher scheme as well as promoting breastfeeding and good weaning practice. Vitamins drops of vitamins A,C, and D are also available free of charge for children who are eligible.

The scheme which is available to pregnant women and those with children under the age of five, who are: eligible for income support; income based job seekers allowance; and child tax credit, (but not working tax credit) and on an income of less than £13, 910 a year.  Pregnant women under 18 qualify whether or not they are claiming benefits.

The vouchers are worth £2.80 week per pregnant woman/ child, except where the child is under the age of 1 year when two vouchers are given each week, a total of £5.60.  The same benefits are available to mothers who are breastfeeding as for those who are not.

Sure Start Children's Centres are designed to offer support to young disadvantaged families, and it planned that by 2010, all local communities will have accessible to Sure Start Childen's Centres . Sure Start also encourages and supports women in breastfeeding, promotes good weaning practices and a healthy diet for young children.

Programmes such as Sure Start and Healthy Start are therefore ideally places to address the issues described in this section, and will be key players in implementing the recommendations from this Guidance.

## 3.4   References for background

Department of Health (1994) *Weaning and the weaning diet.* Report on Health and Social Subjects. Report of the Working Group on the Weaning Diet of the Committee on Medical Aspects of Food Policy, No 45. London: HMSO.

Department of Health (2005a) *Choosing Better Oral Health: an oral health plan for England.* TSO: London.

Department of Health, (2005b). *Choosing a better diet: a food and health action plan.* TSO: London

Department of Health, (2005c) *Choosing Health: Making healthy choices easier* TSO: London

Gregory, J.R, Collins, D.L, Davies, P.S.W, Hughes, J.M., Clarke, P.C. (1995). *National Diet and Nutrition Survey: Children aged 11/2 to 41/2.  Volume 1: Report of the diet and nutrition survey.*  London: HMSO

# 4 Methodology

## 4.1 Literature search

The Centre for Reviews and Dissemination, University of York (Julie Glanville and Dave Fox) conducted the searches for this rapid review in April 2006, with input from the MCN-CC review team (SEK). Initially, a scoping search was undertaken in order to direct and refine the final search strategy. A combined strategy was developed from the draft strategies for infants (6-24 months), and preschool children (2 years to 5 years). All of the searches were conducted using a stepped approach to identify relevant systematic reviews (SRs), randomised controlled trials (RCTs) and non-randomised studies (cohorts, qualitative studies and surveys). A worldwide search of a number of databases was conducted to identify relevant SRs (from 1995 onwards). Secondly, a worldwide search for RCTs was conducted (from 1990 onwards). Finally, the search included any type of study – but this search focused on studies from the UK published from 1990 onwards. Studies not published in English were excluded from the review. These searches were updated by Julie Glanville in January 2007. A detailed report of the processes, databases and search terms used in this rapid review is presented in Appendix A.

Citations identified by the two searches are shown in the table below:

|              | SRs | RCTs | UK studies | Totals |
|-------------|-----|------|------------|--------|
| April 2006   | 693 | 5937 | 1681       | 8311   |
| January 2007 | 189 | 894  | 150        | 1233   |
| Totals       | 882 | 6831 | 1831       | 9544   |

As part of the NICE public health guidance process (NICE, 2004) a stakeholder consultation on the draft summary of evidence was undertaken. This closed on 3rd May 2007. As part of this consultation, stakeholders and Programme Development Group (PDG) members were invited to submit evidence of relevance to this guidance. Any material submitted by stakeholders/ PDG during this consultation was assessed for its relevance using standard NICE criteria (NICE, 2004). As a result of this consultation one paper was included which provided follow up for a RCT of a dietary strategy to reduce allergies (Hide et al, 1996) for which two papers had already been identified. Three UK studies were of interest although they did not include specific relevant interventions and were therefore briefly described in this review (Alder 2004, Anderson 2001, Bolling 2007).

The final totals for included papers therefore became 12 studies (15 publications) which met the inclusion criteria (five SRs, and seven RCTs) and 10 corroborative UK studies. A list of included papers are shown in Appendix B and list of excluded studies with reasons of exclusion in Appendix C.

## 4.2 Selection of studies for inclusion

### 4.2.1 Participants

Participants were infants and young children (approximately 6 to 24 months of age) who were no longer predominantly milk fed. Studies of children with clinical conditions requiring specialist advice, secondary dietary management or clinical therapeutic advice, where normal care would be inappropriate, were excluded (for example, children with established atopic disease). To be included in the rapid review, the studies had to be conducted in developed countries.

Where data were available, the review considered the following population subgroups:
- Children living in areas of deprivation including inner city areas
- Children in black and minority ethnic groups
- Children of mothers aged under 18

### 4.2.2 Interventions

The review included public health interventions that aimed to promote safe and healthy feeding practices.  Studies of interventions that began before the infant was 6 months old were included provided outcomes were reported during the infant's first 24 months of life.  Studies that used a maternal intervention to achieve a child health outcome (for example, iodine supplementation during pregnancy to prevent neonatal hypothyroidism, or maternal dietary restriction as a single intervention to reduce atopy among infants) were excluded from this rapid review.  Studies of uptake of recommended vitamin and mineral supplementation were included, but not studies of effectiveness or dosage of vitamins, minerals or micronutrients, nor of fortification.  Studies of screening interventions were excluded as were any studies on obesity.

Interventions of interest were those promoting:
- Timely introduction of appropriate supplementary feeds/solids
- Introduction of appropriate family foods
- Continuation of breastfeeding after 6 months, especially after the mother had returned to paid employment
- Diet (of the child) to reduce food allergies and intolerance
- Dental health

### 4.2.3 Outcomes

Various outcomes were included depending on the intervention examined.  These included:
- Dietary intake, nutrient and micronutrient intake, nutrient status
- Breastfeeding duration beyond 6 months
- Appropriate provision of foods by mothers, for example, milk, meat and fruit
- Uptake of recommended dietary and micronutrient supplements

Two reviewers independently screened all 9544 titles and abstracts identified in the literature searches.  For this rapid review, full paper copies of 63 SRs, 79 RCTs and 25 UK studies were obtained and independently assessed by two reviewers.  Any disagreements regarding whether or not a paper met the inclusion criteria were resolved in consultation with a third reviewer.

## 4.3   Quality appraisal

All of the studies that met the inclusion criteria were critically appraised by two reviewers in accordance with criteria described in NICE (2004).  A study was graded using a code '++', '+' or '-', based on the extent to which the potential sources of bias had been minimised.  If there was any discrepancy in a grade given to a study by the two reviewers, the opinion of a third reviewer was sought.  It is noted that these grades reflect the quality of the authors' *reporting* of their study.

For the relevant individual studies contained within SRs, the quality grading given by the author of the SR has been quoted and not the NICE quality grade, as we did not have direct access to all the individual studies. Details of the quality assessment

method used in the SRs have been given within the text and within the Evidence Tables.

## Current NICE Grading Scheme

**From:** NICE (2004). *Guideline Development Methods. Information for National Collaborating Centres and Guideline Developers.* London: National Institute for Clinical Excellence (NICE). www.nice.org.uk

**Table 7.1 Levels of evidence for intervention studies.** Reproduced with permission from the Scottish Intercollegiate Guidelines Network; for further information, see 'Further reading'.

| Level of evidence | Type of evidence |
|---|---|
| 1++ | High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias |
| 1+ | Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias |
| 1− | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias* |
| 2++ | High-quality systematic reviews of case–control or cohort studies<br><br>High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+ | Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2− | Case–control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal* |
| 3 | Non-analytic studies (for example, case reports, case series) |
| 4 | Expert opinion, formal consensus |

*Studies with a level of evidence '–' should not be used as a basis for making a recommendation (see section 7.4)

**Grading of evidence**

| | |
|---|---|
| ++ | All or most of the quality criteria have been fulfilled<br><br>Where they have been fulfilled the conclusions of the study or review are thought *very unlikely* to alter |
| + | Some of the criteria have been fulfilled<br><br>Where they have been fulfilled the conclusions of the study or review are thought *unlikely* to alter |
| - | Few or no criteria fulfilled<br><br>The conclusions of the study are thought *likely or very likely* to alter |

Source: NICE, 2004

## 4.4   Study categorisation

The twelve included studies were reported in fifteen papers. Two SRs assessed studies of dental health promotion; two SRs included assessments of interventions to improve children's diets; one SR and six RCTs (reported in nine papers) evaluated dietary strategies (with or without non-dietary strategies) that aimed to reduce the risk of food allergies and intolerance; and one RCT evaluated the effectiveness of interventions that were designed to help mothers continue breastfeeding and reported breastfeeding outcomes when the baby was 6 or more months old.  The included studies are presented by these four types of intervention.

## 4.5  Assessing applicability

Each included study was assessed to determine its applicability to UK settings. Notes on applicability are presented in the data extraction tables.  In addition, a search was conducted for non-randomised UK studies from 1990 onwards to identify corroborative implementation studies of interventions included in the review.  Key points from five such studies have been summarised in tables under the relevant type of intervention.


## 4.6  Synthesis

Due to heterogeneity of design among the studies, a narrative synthesis was conducted.

# 5   Summary of findings

From 9544 titles and abstracts identified in the literature search, full paper copies of 63 SRs, 79 RCTs and 25 UK studies were obtained for this rapid review.

In total, twelve studies met the inclusion criteria (five SRs and seven RCTs, which were reported in fifteen papers).  In addition, seven corroborative UK studies have been included.  These UK studies have not been data extracted, but their key points have been summarised below. As a result of the NICE consultation one further paper providing follow-up from a RCT already included in the review (Hide 1996) was identified and three further UK studies bringing the total number of corroborative UK studies to ten.

Of the twelve included studies, two SRs were concerned with dental health promotion; two SRs included assessments of interventions to improve children's diets (one of which gave very limited data on interventions to promote uptake of recommended vitamin and micronutrient supplements); one SR and five RCTs (reported in seven papers) evaluated baby milk formulas (with or without other dietary or non-dietary strategies) and one RCT (reported in two papers) the use of probiotics that aimed to reduce the risk of food allergies and intolerance; and one RCT evaluated the effectiveness of an interventions that was designed to help mothers continue breastfeeding and reported breastfeeding outcomes when the baby was 6 or more months old.
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## 5.1   Key question 1:

*What interventions effectively promote the timely introduction of appropriate solid/family foods?*

Two SRs addressed aspects of this question.

The primary objective of the SR (quality rating 2+) by Elkan et al. (2000) was to examine the effectiveness of home visiting by health visitors.  Four studies were included that examined children's diet as an outcome variable (Gutelius et al. 1977; Barker et al. 1988, 1994; Johnson et al. 1993). Elkan et al. quality scored these studies using the Reisch quality scale, on which 0 indicates the worst possible and 1 the best.

In the US study by Gutelius et al. (1997) (Reisch quality score 0.59) first-time African-American mothers (aged 15 to 18 years) from low-income families received a total of nineteen home visits (by a paediatrician or nurse) from when a woman was seven months pregnant and during the first three years of the infant's life (n=49) (with nine, six and four visits in the $1^{st}$, $2^{nd}$ and $3^{rd}$ years, respectively) compared to no home visits (n=48).  The authors reported significantly better eating outcomes in the intervention group compared with controls, including appropriate daily milk at 12 months ($p<0.01$), daily meat at six months ($p<0.05$), and fruit servings at 2 and 3 years ($p<0.05$).

Barker and Anderson 1988 (Reisch quality score 0.46) and Barker et al 1994 (Reisch quality score 0.46) evaluated the effectiveness of monthly visits by health visitors in children three to 27 months old, living in the British Isles.  Outcomes included the percentage of children with nutritional intakes less than 50% of the RDA, and the % with an adequate diet.  No statistical tests were reported for these studies, and the results were inconsistent.

The latter two studies in the early 1980s used the Child Development Programme developed at the Early Childhood Development Unit, Bristol, which was extended for 'community mothers' in the Johnson et al. study in 1984.

An Irish study (Johnson et al. 1993) (Reisch quality score 0.25), examined the effectiveness of monthly visits during the first year of a child's life by trained non-professional community mothers (n=141) compared to routine care by health visitors (n=121). The participants in this study were first-time mothers living in an economically deprived area of Dublin. Significantly more women in the intervention group were giving their children a more appropriate diet (as measured using a number of different outcomes). This study was also reported in the review by Tedstone et al. (1998).

Elkan et al. 2000 concluded that this evidence may be subject to bias since the studies relied on maternal self-reports to assess diet, and that overall, there was insufficient evidence to provide any conclusions regarding the impact of home visiting on children's diet.

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*Strength and applicability of evidence*

One 2+ SR (Elkan et al. 2000) evaluated evidence from three RCTs and one non-RCT and concluded that there was insufficient evidence to assess the effectiveness of home visiting on children's diet.

The highest quality study within this SR (Gutelius et al. 1997) (a RCT, Reisch quality score 0.59) found intensive home visiting of low income African American families by a health professional (paediatrician or nurse) in the first 3 years of life significantly improved appropriate intake of daily milk at 12 months, daily meat at six months, and fruit servings at 2 and 3 years.

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The SR by Tedstone et al. (1998) (quality rating 2++) evaluated the effectiveness of interventions to promote healthy feeding of infants under one year of age. Six studies of weaning and post-weaning interventions were included (reported in seven papers: McEnery et al. 1986; Frank et al. 1987; Lapinleimu et al. 1995 and Niinikoski et al. 1996; Griffiths et al. 1995; Childs et al. 1997; Johnson et al. 1993). Tedstone et al. quality rated these studies as good/moderate/poor.

McEnery et al. (1986) (poor/moderate) randomised 69 pregnant Asian women, born on the Indian subcontinent or in East Africa and attending a general practice in East London, UK (Waltham Forest). Socioeconomic details of the participants were not reported. The intervention was a series of 12 culturally specific prenatal health promotion lectures, at the health centre, from a health visitor, midwife or nutritionist with a translator. Appropriate literature was provided and discussion encouraged. The control group received routine prenatal care including mothercraft classes in English in the hospital maternity unit. Attendance at classes was poor and analysis was not by intention to treat. When the children were one year old no effect was found on biochemical indices of their nutrient status, including haemoglobin levels and blood count.

Frank et al. (1997) (good) recruited 343 women, predominantly low-income and non-white, during their postpartum stay in Boston City Hospital (USA). The women were randomised into four groups and received either routine or research breastfeeding counselling with either a commercial or a routine discharge pack. Research

counselling was found significantly to delay the first introduction of solid foods to the infant's diet from median age 91 to 105 days (p=0.03).  The research discharge pack was found significantly to delay daily solid feedings from median age 112 to 120 days (p=0.017).

A Finnish study (reported in two papers, Lapinleimu et al. 1995 and Niinikoski et al. 1996) (moderate/good) randomised families of 1062 children attending well-baby clinics to intensive, individualised health education aimed at decreasing children's exposure to coronary heart disease risk factors by reducing their intake of dietary fats, or to routine care with no detailed input about dietary fats.  No socioeconomic data were presented for the infants, and the recommended nutrient intakes in this study were below UK recommendations.  Lipid levels were measured at time points up to 3 years and the intervention reduced serum lipids and cholesterol levels in both boys and girls up to age 3 years (significant only for boys).  Follow-up was 31% at 3 years.  Intervention children were found to consume less fat and saturated fat than control children and their relative intakes of fat (as % energy) and cholesterol were also lower throughout the intervention.  However, the nutritional objectives of this intervention are beyond those currently considered appropriate for young children in the UK (Department of Health 1994, in Tedstone et al 1998).

The focus of the small, non-randomised trial by Griffiths et al. (1995) (moderate) was on improving intakes of iron-rich foods and vitamin C to prevent anaemia.  Participants were 6-12 month old infants of mainly Asian families of low socio-economic status, from general practices in Bolton, UK.  Parents of intervention group children (n=34) received health promotion from a health visitor, with a translator if required, both face-to-face and via written materials presented in appropriate languages, plus fortnightly visits until the child was 1 year old.  The control group received standard care (not described, n=?).  Mean haemoglobin, anaemia and diet scores that may favour the intervention group are reported at one year without significance tests.  Tedstone's assessment is that a larger study would be required to assess whether the results were not simply due to chance.

Childs et al. (1997) (moderate) also focused on promoting improved intakes of iron-rich foods and vitamin C, alongside good weaning practices, to prevent anaemia.  The participants were 1000 infants (Asian 75%, Afro-Caribbean and white) from two socio-economically deprived areas of Birmingham (UK).  The intervention involved three home visits from a health visitor (at 3, 6 and 9 months) where specific dietary advice was given in relevant languages via audiotapes and in written form.  The control group received standard nutrition education from their own health visitor.  Attrition rates were high (54.5% lost to follow-up).  At 18 months no significant differences were found between the groups in rates of anaemia (27.7% in the intervention group and 26.8% in the control group), dietary intakes of iron or growth data.

Johnson et al. 1993 (also reported by Elkan et al. 2000, with a Reisch quality score of 0.25, see above) appears in Tedstone et al.'s review with the quality rating 'moderate'.  Tedstone et al.'s review reports that the volunteers supported mothers through empowerment, with no specific advice given.  Intervention group infants were significantly less likely to have been given cow's milk before 26 weeks than control group infants (p<0.001).  As measured by the mothers' dietary recall, more intervention group children were given recommended amounts of animal and non-animal protein, whole foods, fruit, vegetables and milk at one year (p<0.01).  Tedstone et al. state these results should be considered with caution.

Tedstone et al. (1998) concluded that the studies reported by Frank et al. 1987, Lapinleimu et al. 1995 and Niinikoski et al. 1996, and Johnson et al. 1993 do not provide an adequate basis for planning future interventions.  Further, Tedstone et al. (1998) was concerned by the failure of the three interventions that targeted high-risk groups in the UK (McEnery et al. 1986, Griffiths et al. 1995 and Childs et al. 1997) to reduce the prevalence of anaemia, pointing out the importance of identifying barriers to improving the iron status of high-risk groups and how to address them.

Tedstone et al. (1998) recommended that: "Research on the promotion of optimal weaning and post-weaning feeding practices in the UK should focus on:
- developing effective promotional programmes on optimal weaning practices for the UK setting
- interventions that specifically delay to 4 months of age (sic) the introduction of solids, increase the intake and availability of iron, reduce the use of unmodified cow's milk, reduce the use of non-milk extrinsic sugars and increase the variety of weaning foods, and
- those at greatest risk of developing nutritionally related health problems such as iron deficiency, anaemia and dental caries."

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*Strength and applicability of evidence*
One 2++ SR (Tedstone et al. 1998) evaluated evidence from five RCTs and one non-RCT and found that there was insufficient evidence to make recommendations about optimum weaning and post-weaning dietary practices.

A study within this SR (graded 'moderate' by the reviewers) found monthly visits by 'community mothers' significantly improved dietary intake of animal protein, non-animal protein, whole foods, milk, fruit and vegetables in infants under one-year of age from low-income families in Dublin (Johnson et al. 1993).

A large Finnish RCT within this SR (Lapinleimu et al. 1995, Niinikoski et al. 1996) (graded 'moderate/good' by the reviewers) found specific dietary counselling and health education conducted in a health clinic reduced serum lipids and cholesterol levels in both boys and girls up to the age 36 months (significant only for boys) and was successful in reducing dietary intake of fat, saturated fat in both girls and boys up to age 36 months.  However, the nutritional objectives of this intervention are beyond those currently considered appropriate for young children in the UK.

A US RCT in the Tedstone et al. SR (Frank et al. 1997) (graded 'good' by the reviewers) in predominately non-white and low-income mothers during their post partum hospital stay and with two separate interventions found both research counselling (p=0.03) and a research discharge pack (p=0.02) delayed the introduction of solid foods by 14 and 8 days, respectively.

Three studies within this SR (two RCTs (Childs et al. 1997, McEnery et al. 1986) and one non-randomised controlled trial (Griffiths et al. 1995), all graded 'moderate' by the reviewers) evaluated three different interventions including home visiting by health visitors and health education. The studies found no effect on the incidence of anaemia in children under 18 months of age from predominantly Asian low-income families living in the UK.

### 5.1.1  Corroborative UK evidence

**Timely introduction of appropriate solids/family foods**.

**Anderson et al. 2001**

Anderson et al. (2001) surveyed twenty-nine mothers from more deprived backgrounds in a Scottish maternity hospital setting. Five groups of mothers (with 5-7 participants) (mean age 27.0 ± 4.8 years) with babies aged 8-18 weeks (mean age 13.0 ± 4.2 weeks) took part in focus group discussions lead by a psychologist research assistant about their babies' feeding habits for ~1.5 hours. Primiparous (22) and multiparous (7) mothers were separated except for one focus group. Ten of the 29 participants had already introduced solid food to their infants at a mean age of 11.6 weeks (range 2-16 weeks) although the current guidelines recommended not introducing solids before 4 months. All mothers were aware of the current recommendations but few knew why and found it difficult to understand the concept of long-term health. Mothers believed that the introduction of solids should be baby led and initiated by some physical characteristic or behavioural action of the infant. The conflict between rigid feeding guidelines and flexible advice from supportive health professionals created confusion over the importance of good weaning practices. The authors recommended further research in order to design relevant intervention strategies.

**Alder et al. 2004**

A prospective cohort study in Fife, Scotland in 1999 of primiparous women aged 16 to 40 years (N=526) was of relatively affluent predominately white women (deprivation category scores of 3 or 4). In 1999 the recommended age for the introduction of solids was four months, and therefore at 12 weeks post partum 338 of 448 women (76%) were interviewed at which time 40% (133/338) had introduced solids, although 13% (43 women) had stopped and started. Most (60%) said that they intended giving solids at 16 weeks but 11% (23) said when their children were ready and 2% (7) had not thought about it. Sixty four per cent (286/448) returned a postal questionnaire at 20 weeks post partum when 95% (272/286) had given solids to their babies and 97% reported the age when solids had been given. Early introduction of solids (at <12 weeks) was associated with: having a male baby (OR 2.01, 95% CI 1.26, 3.21); smoking during pregnancy (OR 3.27, 95% CI 1.90, 5.60); being a younger mother (age <20 years) (OR 2.50, 95% CI 1.21, 5.20); the opinion of the maternal grandmother; living in a deprived area (deprivation score, p<0.05); personal disagreement with the advice to wait to introduce solids until 4 months (p<0.05); lack of encouragement from friends to wait until age 4 months (p<0.05); and being in receipt of free samples of manufactured food (OR 2.74, 95% CI 1.70, 4.43). The authors commented that some of the factors were amenable to change and could be targeted in educational interventions.

**Hoare et al. 2002**

All mothers of babies born in two market towns in Northumbria during the study period were invited to take part in this non-randomised study, and approximately one-third participated.  Participants were parents of 8-week old infants who attended one of several discussion groups in their town on weaning (intervention, n=61) or home safety (control, n=49).  One single-parent family was included, and the sample was not matched for social class, with 26% of the intervention group and 10% of the

control group reporting a manual occupation.  All the discussion sessions started with a quiz that included questions about weaning.  The intervention sessions were loosely structured to cover the main points of the COMA report (Weaning and the weaning diet, DH 1994).  Parents in both groups were asked by their family health visitor to complete a questionnaire that included questions about weaning at their infants' 7-9-month development checks.  Parents in the intervention group reported using more home-cooked foods (p=0.0034) and fewer commercially prepared baby foods (p=0.0013), and more knew the optimum time to register their infants with the dentist (p=0.03) compared with controls, despite the greater affluence and implied higher educational attainment of the control group.  The authors conclude that participant-centred discussions on infant feeding were an effective mode of disseminating Government recommendations in Northumberland, and recommend that postnatal groups incorporating infant feeding discussions be available as routine service provision.

**Sritharan and Morgan, 2002**

The authors analysed five infant recipe books obtained from online and high street booksellers.  From each book, a 24h menu was devised, based on the recipes and practical advice provided by each author, for infants aged 6-9 months.  The nutrient composition of each cookbook's menu varied enormously.  The paper reports content of energy, protein, carbohydrate, sugars, fat, NSP, vitamin A, vitamin C, calcium, iron and sodium in the 24h diet from each book, but does not compare these with RDAs. They state that sodium levels were particularly high in three menu plans (at 1047 mg, 912 mg and 690 mg).  The authors state the results of their study expose the poor nutritional practice that exists in an unregulated market.  They consider there is a danger that some books may present more of a risk than a remedy on the issues of parental understanding of appropriate infant feeding practices.  They suggest this may be an area where regulation should be considered.

**Timely introduction of appropriate solids/family foods/follow-on formula/allergenic foods/breastfeeding outside the home or at work.**

**Bolling et al. 2007**

A UK Infant Feeding Survey on behalf of The Information Centre for health and social care and the UK Health departments by BMRB Social Research, of children born in August and September 2005 aimed to determine the incidence, prevalence and duration of breastfeeding and other feeding practices at 4-10 weeks old (stage 1), 4-6 months old (stage 2) and at 8-10 months old (stage 3). (This is the 7th of the five-yearly national surveys.) A total of 9416 mothers in the representational sample completed all 3 questionnaires at stages 1, 2 and 3. Forty eight per cent of women were breastfeeding at 6 weeks and 25% at 6 months. In England, Wales and Northern Ireland breastfeeding had increased at all ages but only at ages up to 6 weeks in Scotland. A negligible proportion of mothers (<1%) were exclusively breastfeeding at age 6 months. At stage 2 use of follow-on milk or liquid cow's milk was low.  At stage 3 about half of all mother's had given follow-on milk and most had followed the recommendation of not giving follow-on milk before age 6 months, although mother's from routine and manual occupations, who had never worked, and with the lowest educational level were most likely to have given follow-on milk at an earlier age. Just under half of mothers who had prepared formula had not followed key recommendations by either not always using boiled water that had cooled for <30 minutes or not always adding the water to the bottle before the powder. About a third of mothers did not follow the recommendations for preparing formula when away

from the home, either by not keeping prepared formula chilled or by using cold or cooled water when making up feeds.

Factors relating to breastfeeding outside the home were also assessed. By stage 3, 45% mothers had returned to work. Eighty percent of mothers returning to work did so after their baby was 5 months old, with 57% returning after their baby was 6 months old. Most mothers worked part-time: 14% working <15 hours per week and 56% working 15-30 hours per week. One in seven mothers was provided with facilities to either express milk or breastfeed at work, which were particularly associated with the use of a workplace crèche. Mothers were more likely to be working and breastfeeding at 5-6 months if they were working <15 hours per week, in managerial or professional occupations, or given access to facilities for breastfeeding or expressing milk at work. Eighty six per cent of mothers breastfeeding at ≥6 months had breastfed in public. Three per cent of mothers had been asked not to breastfeed in public although 13% had been made to feel uncomfortable. Eight per cent of mothers said that they had wanted to breastfeed in public but had been deterred from doing so. Mothers in Scotland had more positive experiences when breastfeeding in public.

Mothers were continuing a long-term trend in all 4 countries and introducing solids later in 2005 than in 2000. For example, 51% mothers in 2005 had introduced solid foods by 4 months but the percentage was 85% in 2000. Solid foods were introduced earlier in Wales and Scotland and by mothers in the lower social classes and with lower education levels. Solids given at age 4-6 months were more likely to be commercially-prepared than home-prepared foods but at 8-10 months there was increased use of home-prepared foods. A large proportion of mothers of stage 3 infants avoided the use of salt completely. Salt was more likely to be used by mothers in the lower occupational groups and in ethnic minority groups. A higher proportion of mothers in 2005 than 2000 avoided the use of salt, nuts and honey – one of the key reasons being a greater awareness of food allergies.


## 5.2  Key question 2:

*What interventions effectively promote uptake of recommended vitamin and micronutrient supplements?*

Three studies within the Tedstone et al. SR (2++) (two RCTs (Childs et al. 1997, McEnery et al. 1986) and one non-randomised controlled trial (Griffiths et al. 1995), all graded 'moderate' by the reviewers) evaluated three different interventions including home visiting by health visitors and health education for predominantly Asian low-income families living in the UK. All three interventions had no significant effect on the incidence of anaemia in children less than 18 months of age. The interventions are described above in the section relevant to Key question 1: *What interventions effectively promote the timely introduction of appropriate solid/family foods?* It is not clear whether all three study interventions promoted the uptake of recommended vitamin and micronutrient 'supplements' but two studies focussed on improving intakes of iron-rich foods and vitamin C (Childs et al. 1997, Griffiths et al. 1995). The RCT by McEnery and Rao (1986) had a wider focus which included 'child-rearing issues' but did compare vitamin supplement intake after the intervention.

The UK RCT by Childs et al. (1997) in Birmingham focused on promoting improved intakes of iron-rich foods and vitamin C, alongside good weaning practices, to prevent anaemia.

For the RCT (graded poor/moderate by the reviewer) by McEnery and Rao (1986) the focus was prenatal pregnancy and child health promotion in women born in India or Asians from East Africa living in Waltham Forest, London. Fertility, pregnancy, child birth, child-rearing issues and breastfeeding promotion but not breastfeeding issues were covered in the prenatal lectures. At age one year dietary histories were taken from the children, anthropometric measurements made and haemoglobin, red cell count, serum calcium, phosphate, magnesium, alkaline phosphatase and 25-hydroxyvitamin D measured. The intervention failed as attendance at the classes was poor: only 46% (16/35) women in the intervention group attended ≥4 of the 12 classes (and these were considered to be the more educated group) so the remainder were moved to the control group. Loss to follow-up varied and differed for individual biochemical measurements but was 25% for the anthropometric data and 38% for breastfeeding data. Vitamin supplements were given to 94% (33/35) of the intervention infants and 86% (29/34) of the control infants. Haemoglobin level was slightly higher in the control group (11.9 g/dl) than the intervention group (11.1 g/dl). The authors suggested that health education in the home may be more appropriate for these women since their large families and poor English made regular attendance at a clinic difficult.

The focus of the small, non-randomised trial by Griffiths et al. (1995) (moderate) was on improving intakes of iron-rich foods and vitamin C to prevent anaemia by giving dietary advice. Parents of intervention group children (n=34) aged 6-12 months from mainly Asian families in Bolton were shown a health promotion display illustrating iron rich foods and given one-to-one advice on suitable foods and recipes by the community health and food advisor, with weaning leaflets in appropriate language with advice and recipes. Parents were then visited bi-monthly for 12 months. Diet was assessed using a food frequency questionnaire every 2 months from baseline and followed using a scoring system and haemoglobin and serum ferritin levels measured. Mean haemoglobin, anaemia and diet scores favoured the intervention group but no significance levels were given. The intervention may have been successful but the study was too small for the results to reach significance.

### 5.2.1 Corroborative UK evidence

**Cleghorn et al. 2006**

Rickets affects mainly dark-skinned infants being breastfed for prolonged periods without vitamin supplementation. A UK cross-sectional study of 98 health visitors (HV) in the Brent, Harrow and Westminster Primary Care Trusts in 2002 (response rate 69%) assessed the HV's knowledge of the government guidelines for vitamin supplementation for infants and children and the advice given to mothers. The official government guidelines were: vitamins from age 6 months if breastfed; vitamins from age 1 month if breastfed and there is doubt about mother's nutritional state during pregnancy; vitamins if the baby is on formula-milk and drinking <500 ml/day; vitamins when the child is drinking cow's milk as a main drink; vitamins until age two years if the child is at risk of vitamin D deficiency and the diet is not diverse and plentiful, in which case continue vitamin supplementation until age five years. Seventy nine HVs (81%) recommended vitamins for the breastfed infant at ≤6 months, 18 of which recommended vitamin supplementation at age one month. Fifty six HVs (57%) recommended vitamin supplementation until age five years. Seventy nine HVs (81%) correctly identified Asians at being at risk of developing rickets but only 28 (29%) and 16 (16%) HVs, respectively, identified Black Africans and Black Caribbeans to be at risk. The study concluded that the majority of HVs were following the correct government guidelines but greater awareness needed to be raised to ensure that all

HVs were imparting consistent, correct advice for vitamin D supplementation for ethnic minorities.


## 5.3   Key question 3:

*What dietary strategies effectively reduce the risk of food allergies and intolerance?*

One SR and five RCTs (reported in seven papers) evaluated baby milk formulas (with or without non-dietary strategies) and one RCT (reported in two papers) the use of probiotics that aimed to reduce the risk of food allergies and intolerance. The literature search also identified one potentially relevant SR by Ram 2002. However, a number of the meta-analyses included work by Chandra (recently discredited). Relevant RCTs included in the SR by Ram were identified in the search for this rapid review, and were assessed individually.

### 5.3.1   Probiotics

A single Finnish RCT (quality rating 1+) reported in two papers (Kalliomaki et al. 2001; 2003) evaluated the effectiveness of probiotics in the prevention of early atopic disease in children at high risk (N=159).  Participants were infants of mothers recruited in antenatal clinics, who had at least one first degree relative (or partner) with atopic eczema, allergic rhinitis or asthma.  Socio-economic background of the mothers was not reported.  Intervention group mothers initially received two capsules of colony-forming units of the probiotic *Lactobacillus rhamnosus* strain GG daily from two weeks before expected date of delivery.  Breastfeeding mothers took the capsules daily for six months after the birth, or gave the capsule contents diluted with water to their infant with a spoon.  The control group received a placebo.  Follow-up was 83% in both groups.  Among those who completed the study, the frequency of atopic eczema was significantly reduced in the infants in the intervention group (15/64, 23%) compared with controls (31/68, 46%) (p=0.008, RR 0.51, 95% CI 0.32, 0.84, number needed to treat 4.5).  There were no significant differences in the other measured indicators of atopic disease.

> *Strength and applicability of evidence*
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> A single RCT (1+) (Kalliomaki et al. 2001; 2003) examined the effect of giving Lactobacillus GG to breastfeeding mothers from atopic families or their infants. Mothers received two capsules of $10^{10}$ Lactobacillus GG daily for two weeks prior to delivery and postnatally for six months. Infants were given the capsule contents diluted with water on a spoon. The incidence of atopic eczema in children was significantly reduced up to 4 years of age, whether capsules were given to the breastfeeding mother or infant. There were no significant differences in other indicators of atopic disease.

### 5.3.2   Formula and allergenic foods

One SR (Osborn and Sinn 2006) and five RCTs (reported in seven papers: Arshad 1992, Hide 1994, Hide 1996, Odelram 1996, Oldaeus 1997, Schonberger 2005, Von Berg 2003) evaluated baby milk formulas (with or without non-dietary strategies) that aimed to reduce the risk of food allergies and intolerance. Two of the RCTs were also included in the SR (Oldaeus 1997, Von Berg 2003).

A SR (2++) by Osborn and Sinn (2006) assessed the use of formula containing hydrolysed protein for prevention of allergy and food intolerance in infants and included eighteen studies (13 RCTs and 5 quasi-randomised trials: Chirico 1997, de

Seta 1994, Halken 2000, Juvonen 1996, Lam 1992, Maggio 2005, Mallet 1992, Marini 1996, Nentwich 2001, Oldaeus 1997, Picaud 2001, Saarinen 1999, Szajewska 2001, Tsai 1991, Vandenplas 1992, Vandenplas 1993, Von Berg 2003, Willems 1993). Five of the 18 studies (Maggio 2005, Oldaeus 1997, Szajewska 2001, Tsai 1991, Vandenplas 1993) were considered to have adequate methodology, which was prespecified as: adequate randomisation and allocation concealment and <10% losses to follow-up. Interventions included the use of hydrolysed infant formulas including hydrolysed cow's milk and soy formulas, and extensively and partially hydrolysed formulas. Hydrolysed formulas could be used for: 1) early short term supplementary feeds or sole formula feeding in infants unable to be breastfed in the 1$^{st}$ few days; or 2) for prolonged supplementation or sole formula feeding in the first months; or 3) weaning from the breast using infant formula. Control groups included infants who received exclusive human milk (either breastfed or expressed) or an adapted cow's milk formula. Comparisons were made for hydrolysed formula, partially hydrolysed formula, and extensively hydrolysed formula; and between early (short term) feeding and prolonged feeding. Most studies were of infants at high risk of atopy but five studies were of a 'normal' infant population (Juvonen 1996, Maggio 2005, Picaud 2001, Saarinen 1999, Szajewska 2001) and one study of infants at low risk of atopy (Vandenplas 1993).

For <u>hydrolysed formula versus exclusive human milk</u> there were just two studies of early short term feeding in low risk infants giving no significant difference in any allergy at age 3 years (Juvonen 1996) or for cow's milk allergy at 27 months (Saarinen 1999). The authors concluded that "There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy compared to exclusive breastfeeding".

For <u>hydrolysed formula versus cow's milk formula</u>, the same two studies of early short term feeding gave no significant difference in any allergy at age 3 years (Juvonen 1996) but a significant reduction in cow's milk allergy at 27 months, RR 0.62, 95%CI: 0.38, 1.00; RD -0.01, 95%CI: -0.02, 0.00 (Saarinen 1999).

There were ten studies of prolonged feeding of hydrolysed formula versus cow's milk formula in all infants (Chirico 1997, de Seta 1994, Lam 1992, Mallet 1992, Marini 1996, Oldaeus 1997, Tsai 1991, Vandenplas 1992, Von Berg 2003, Willems 1993). In practice all the studies were found to be in high risk infants. There were no studies of prolonged feeding of hydrolysed formula versus cow's milk formula in low risk infants. Meta-analysis for seven studies (de Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993) and incidence of any infant allergy found a significant reduction, RR 0.79, 95%CI: 0.66, 0.94; RD -0.04, 95%CI: -0.08, -0.01, which was also significant for two individual studies (Lam 1992, Vandenplas 1992). Meta-analysis for two studies of prolonged feeding of hydrolysed formula versus cow's milk formula (Marini 1996, Von Berg 2003) found no significant difference in incidence of any childhood allergy but one individual study (Marini 1996) gave a significant reduction, RR 0.42, 95%CI: 0.19, 0.90. No significant reduction was found for incidence of infant asthma (meta-analysis of four studies), childhood asthma (Marini 1996) and childhood asthma prevalence (Von Berg 2003); or infant eczema incidence (meta-analysis of eight studies), childhood eczema incidence (meta-analysis of two studies) and childhood eczema prevalence (Von Berg 2003); or infant rhinitis incidence (Marini 1996); or incidence of food allergy (Oldaeus 1997). However one study of prolonged feeding of hydrolysed formula versus cow's milk formula found a significant reduction in infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89 (Vandenplas 1992). Further analysis using the two studies of hydrolysed formula versus cow's milk formula with adequate methodology (Oldaeus 1997, Tsai 1991) found no significant differences for the only two possible meta-analyses for incidence of infant eczema and infant asthma.

A comparison was also made for studies of prolonged feeding of hydrolysed formula versus cow's milk formula where infants were solely on formula feeding, which included six studies (Chirico 1997, De Seta 1994, Lam 1992, Marini 1996, Vandenplas 1992, Willems 1993). Overall conclusions did not change. Meta-analysis of five studies found a significant reduction in any infant allergy incidence, RR 0.61, 95% CI: 0.46, 0.80 (De Seta 1994, Lam 1992, Marini 1996, Vandenplas 1992, Willems 1993). Meta-analysis found no significant differences in infant asthma incidence (2 studies) or incidence of infant eczema (4 studies).

The authors of the review concluded that: "In high risk infants who are unable to be completely breastfed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula reduces infant and childhood allergy and infant cow's milk allergy." The SR therefore gave 2++ evidence for a reduction in incidence of any infant allergy associated with feeding hydrolysed formula for the first few months versus cow's milk formula.

For extensively hydrolysed formula versus cow's milk formula, there were four studies of prolonged feeding (Mallet 1992, Oldaeus 1997, Szajewska 2001, Von Berg 2003). No individual study showed a significant difference for any allergy, specific allergies or food intolerance. Meta-analyses for incidence of any infant allergy (two studies) and infant eczema (three studies) showed no significant differences. Only one study was of extensively hydrolysed whey formula versus cow's milk formula (Von Berg 2003). Comparisons were also made for three studies of extensively hydrolysed casein formula versus cow's milk formula (Mallet 1992, Oldaeus 1997, Von Berg 2003) where overall results were different from those for extensively hydrolysed formula per se. No significant reduction was found for incidence of any infant allergy (meta-analysis of two studies); incidence of infant asthma (Oldaeus 1997) and prevalence of childhood asthma (Von Berg 2003); or infant rhinitis incidence (Marini 1996); or incidence of food allergy (Oldaeus 1997). Von Berg et al (2003) found with extensively hydrolysed casein formula versus cow's milk formula, a significant reduction in incidence of any childhood allergy, RR 0.72, 95%CI: 0.53, 0.97; incidence of infant eczema, RR 0.69, 95%CI: 0.47, 1.00; incidence of childhood eczema, RR 0.66, 95%CI: 0.44, 0.98; and prevalence of childhood eczema, RR 0.50, 95%CI: 0.27, 0.92. Meta-analysis for incidence of infant eczema (all three studies) also showed a significant reduction for extensively hydrolysed casein formula versus cow's milk formula, RR 0.69, 95%CI: 0.47, 1.00, but the study by Von Berg et al (2003) contributed 75% weight to the meta-analysis.

There were nine studies of prolonged feeding of partially hydrolysed formula versus cow's milk formula (Chirico 1997, De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Tsai 1991, Vandenplas 1992, Von Berg 2003, Willems 1993). Meta-analysis of seven studies (De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993) found a significant reduction for any infant allergy, RR 0.79, 95%CI: 0.65, 0.97, of which two individual studies also showed a significant reduction (Lam 1992, Vandenplas 1992). Meta-analysis of two studies (Marini 1996, Von Berg 2003) showed no significant difference in any childhood allergy – the two studies showed significant heterogeneity with only one study giving a significant difference, RR 0.42, 95%CI: 0.19, 0.90 (Marini 1996). No significant reduction was found for incidence of infant asthma (meta-analysis of four studies), childhood asthma (Marini 1996) and childhood asthma prevalence (Von Berg 2003); or infant eczema incidence (meta-analysis of seven studies), childhood eczema incidence (two studies) and childhood eczema prevalence (Von Berg 2003); or infant rhinitis incidence (three studies with no meta-analysis) and childhood rhinitis incidence (Marini 1996); or incidence of food allergy (Oldaeus 1997). However one study of prolonged feeding of partially hydrolysed formula versus cow's milk formula found a significant reduction in infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89

(Vandenplas 1992). The SR therefore gave 2++ evidence for a reduction in incidence of any infant allergy associated with feeding partially hydrolysed formula for the first few months versus cow's milk formula.

A further comparison was made for studies of prolonged feeding of partially hydrolysed whey formula versus cow's milk formula, which in practice included eight of the nine studies above with the omission of the study by Oldaeus et al (1997). Overall conclusions were not changed. The significant reduction for the meta-analysis of six studies of any infant allergy was RR 0.73, 95%CI: 0.59, 0.90 (De Seta 1994, Lam 1992, Marini 1996, Vandenplas 1992, Von Berg 2003, Willems 1993). The study by Oldaeus et al (1997) of prolonged feeding of partially hydrolysed casein containing formula versus cow's milk formula reported no significant differences for incidence of any allergy. The SR therefore gave 2++ evidence for a reduction in incidence of any infant allergy associated with feeding partially hydrolysed whey formula for the first few months versus cow's milk formula.

Comparison of prolonged feeding of extensively hydrolysed formula versus partially hydrolysed formula was made for four studies (Halken 2000, Nentwich 2001, Oldaeus 1997, Von Berg 2003). No significant differences were found for any individual study or for meta-analyses of incidence of any infant allergy (three studies), incidence of infant asthma (two studies) and incidence of infant eczema (four studies). However, there was a significant reduction in incidence of infant food allergy (two studies), RR 0.43, 95%CI: 0.19, 0.99 (Halken 2000, Oldaeus 1997). The authors concluded that "In view of methodological concerns and inconsistency of findings, further large, well-designed trials comparing formulas containing partially hydrolysed whey, or extensively hydrolysed casein to cow's milk formula are needed."

In summary, the authors concluded that:
- "There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy compared to exclusive breastfeeding.

- In high risk infants who are unable to be completely breastfed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula reduces infant and childhood allergy and infant cow's milk allergy.

- In view of methodological concerns and inconsistency of findings, further large, well-designed trials comparing formulas containing partially hydrolysed whey, or extensively hydrolysed casein to cow's milk formula are needed."

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*Strength and applicability of evidence*

Two studies in the SR (2++) by Osborn and Sinn (2006) compared short term feeding of hydrolysed formula versus exclusive human milk in low risk infants and gave no significant differences for any childhood allergy (Juvonen 1996) or for cow's milk allergy in infants (aged <3 years) (Saarinen 1999).

Two studies in the SR (2++) by Osborn and Sinn (2006) compared short term feeding of hydrolysed formula versus cow's milk formula and gave no significant differences for any childhood allergy (Juvonen 1996) but a significant reduction in infant cow's milk allergy, RR 0.62, 95%CI: 0.38, 1.00; RD -0.01, 95%CI: -0.02, 0.00 (Saarinen 1999).

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There were ten studies in the SR (2++) by Osborn and Sinn (2006) which compared underline prolonged feeding (for the first few months) of underline hydrolysed formula versus cow's milk formula (Chirico 1997, de Seta 1994, Lam 1992, Mallet 1992, Marini 1996, Oldaeus 1997 ('adequate' methodology), Tsai 1991, Vandenplas 1992, Von Berg 2003, Willems 1993). Meta-analysis for seven studies gave a significant reduction for incidence of any infant allergy, RR 0.79, 95%CI: 0.66, 0.94; RD -0.04, 95%CI: -0.08, -0.01 (De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993). Other meta-analyses for prolonged feeding of hydrolysed formula versus cow's milk formula gave no significant difference for any incidence of childhood allergy (two studies), infant asthma (four studies), infant eczema (eight studies) and childhood eczema (two studies). One individual study gave a significant reduction for infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89 (Vandenplas 1992). All the studies were in high risk infants. Further analyses for studies of hydrolysed formula versus cow's milk formula where infants were solely on formula feeding did not change the overall results. The authors of the review concluded that "In high risk infants who are unable to be completely breastfed, there is limited evidence that prolonged feeding with a hydrolysed formula compared to a cow's milk formula reduces infant and childhood allergy and infant cow's milk allergy".

Four studies in the SR (2++) by Osborn and Sinn (2006) compared underline prolonged feeding of extensively hydrolysed formula versus cow's milk formula (Mallet 1992, Oldaeus 1997 ('adequate' methodology), Szajewska 2001, Von Berg 2003) for which meta-analyses gave no significant difference for incidence of any infant allergy (two studies) or infant eczema (three studies). Only one study investigated extensively hydrolysed whey formula versus cow's milk formula (Von Berg 2003). Three studies investigated extensively hydrolysed casein formula versus cow's milk (Mallet 1992, Oldaeus 1997, Von Berg 2003) for which meta-analysis for all three studies gave a significant reduction in infant eczema incidence, RR 0.69, 95%CI: 0.47, 1.00, but the study by Von Berg et al (2003) contributed 75% weight to the meta-analysis. The study by Von Berg et al (2003) also found other significant differences for prolonged feeding of extensively hydrolysed casein formula versus cow's milk formula: a reduction in incidence of any childhood allergy, RR 0.72, 95%CI: 0.53, 0.97; incidence of infant eczema, RR 0.69, 95%CI: 0.47, 1.00; incidence of childhood eczema, RR 0.66, 95%CI: 0.44, 0.98; and prevalence of childhood eczema, RR 0.50, 95%CI: 0.27, 0.92.

Nine studies in the SR (2++) by Osborn and Sinn (2006) compared underline prolonged feeding of partially hydrolysed formula versus cow's milk formula (Chirico 1997, De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997 ('adequate' methodology), Tsai 1991 ('adequate' methodology), Vandenplas 1992, Von Berg 2003, Willems 1993) for which meta-analyses gave no significant differences for incidence of childhood allergy (two studies, which showed significant heterogeneity); infant asthma (four studies); infant eczema incidence (seven studies), childhood eczema incidence (two studies); or infant rhinitis incidence (three studies - no meta-analysis). Meta-analysis of seven studies found a significant reduction for any infant allergy, RR 0.79, 95%CI: 0.65, 0.97 (De Seta 1994, Lam 1992, Marini 1996, Oldaeus 1997, Vandenplas 1992, Von Berg 2003, Willems 1993). One study of prolonged feeding of partially hydrolysed formula versus cow's milk formula found a significant reduction in infant cow's milk allergy, RR 0.36, 95%CI: 0.15, 0.89 (Vandenplas 1992). One of the nine studies was of partially hydrolysed casein containing formula and reported no significant differences for incidence of any allergy (Oldaeus 1997). The remaining eight studies compared prolonged feeding of partially hydrolysed whey formula versus cow's milk formula for which the overall conclusions for partially hydrolysed formula are unchanged.

The SR (2++) by Osborn and Sinn (2006) contained four studies that compared prolonged feeding of extensively hydrolysed formula versus partially hydrolysed formula (Halken 2000, Nentwich 2001, Oldaeus 1997 ('adequate' methodology), Von Berg 2003). No significant differences were found for any individual study or for meta-analyses of incidence of any infant allergy (three studies), incidence of infant asthma (two studies) and incidence of infant eczema (four studies). However, there was a significant reduction in incidence of infant food allergy (two studies), RR 0.43, 95%CI: 0.19, 0.99 (Halken 2000, Oldaeus 1997).

One RCT (quality rating 1+) reported in three papers (Arshad et al. 1992, Hide et al. 1994, 1996) evaluated the effects of a prophylactic intervention on infants with a family history of atopy. In this UK study (N=120), mothers from all socio-economic backgrounds were prenatally randomised to a multi-faceted intervention involving reduced exposure to allergens in food and house-dust mites during the first year of life. After birth, lactating mothers avoided milk, egg, fish and nuts. If necessary, breastfeeds were supplemented with a soya-based protein hydrolysate. Formula fed infants were also given a soya-based protein hydrolysate (Aptamil HA) from birth. Later, the infant's diets were free of cow's milk, egg, wheat, soya, orange, fish and nuts. Cow's milk and soya were introduced at nine months, wheat at ten months, and egg at 11 months. In addition, the infants' bedrooms and living rooms were treated with an acaricidal powder and foam in the first week of life and then every three to nine months (to kill mites), and all infants used polyvinyl-covered mattresses with vented head area. In comparison, the diet of the control group mothers and infants was unrestricted, and there was no acaricidal treatment in the household. At 12 months, 40% of infants in the control group had developed allergic disorders compared to 14% in the intervention group (OR: 6.34, 95% CI: 2.0, 20.1, p<0.005). The prevalence of asthma and eczema at 12 months (7% vs. 19% for both) was also significantly higher in the control group (OR: 4.13, 95% CI: 1.1, 15.5, p<0.05, and OR: 3.6, 95% CI: 1.0, 12.5, p<0.05, respectively). At 12 months, 11% of infants in the control group had a food intolerance (mostly cow's milk or egg) compared to 3% in the intervention group but this result was not significant. Infants from a low socioeconomic group had a higher risk of developing allergy than those from a high socioeconomic group, OR: 3.3, 95% CI: 1.1, 10.2, p<0.05. In a follow-up study at two years (Hide 1994), 26% in the intervention group and 47% controls were found with one or more allergic symptom (any combination of asthma, eczema, food intolerance and allergic rhinitis). Infants in the control group remained more likely to manifest any allergy (p<0.005), and eczema (p=0.008), but the enhanced risk of asthma shown at 1 year was no longer demonstrated. Follow-up at age four years (Hide 1996) found that the control group remained significantly more likely to manifest any allergy (p<0.02), react to a skin-prick test (p<0.02) or have eczema (p<0.05).

*Strength and applicability of evidence*

A single (UK) RCT (1+) in infants with a family history of atopy (Arshad et al. 1992) showed that a package of interventions including reduced exposure to allergens in food for breastfeeding mothers and infants, and a reduced exposure to house dust, reduced the frequency of allergic disorders at twelve months. Parental smoking was a significant risk factor for total allergy as 12 months (p<0.05). Infants from lower socio-economic groups had a higher risk of developing allergy than those from a higher socio-economic group (p<0.05).
Follow-up at ages 2 and 4 years (Hide et al. 1994, 1996) showed that the infants in the control group remained more likely to develop any allergy (p<0.005 at age 2

years; p<0.02 at age 4 years) and eczema (p=0.008 at age 2 years; p<0.05 at age 4 years) but the enhanced risk of asthma was no longer significant.

A Dutch RCT (quality rating 1+) (Schonberger et al. 2005) in infants at high risk of developing asthma (N=476) used a multifaceted intervention in which families received instructions at three home visits from specially trained nurses at 4-6 months pregnant, 8 months pregnant and 1-3 weeks after the birth on how to reduce exposure to mite, pet and food allergens, and passive smoking. The dietary recommendations were to breastfeed for ≥6 months and, if supplementation was necessary or if breastfeeding stopped before age 6 months, to use extensively hydrolysed formula milk and to postpone the introduction of solid foods until age 6 months. Loss to follow-up at age 2 years was 7%. During the first 2 years of life, the incidence of asthma-like symptoms was similar in both groups: however, subanalysis revealed a significant reduction in wheezing (p=0.03), shortness of breath (p=0.01) and night-time cough (p=0.04) in girls, but not in boys. At age 2 years, the intervention group had fewer asthma symptoms, including wheezing (OR 0.73, 95% CI: 0.56, 0.96, p<0.05), shortness of breath (OR 0.76, 95% CI: 0.61, 0.96, p<0.05), and night-time cough (OR 0.72, 95% CI: 0.55, 0.95, p<0.05), than the control group. Multiple logistic regression revealed that exposure to mite allergens, food allergens and passive smoking all contributed independently of each other to asthma symptoms. Feeding hypoallergenic formula or the introduction of solid foods at <6 months were not significantly associated with asthma symptoms at age 2 years or earlier but "ever having breastfed" was significantly negatively correlated with wheezing at age 2 years or earlier (OR 0.42, 95% CI: 0.18, 0.97, p<0.05, at age 2 years; OR 0.32, 95% CI: 0.19, 0.56, p<0.05, up to age 2 years).

*Strength and applicability of evidence*

A single RCT (1+) (Schonberger et al. 2005) in infants at high risk of developing asthma used a multifaceted intervention in which families received instructions from nurses at 4-6 months pregnant, 8 months pregnant and 1-3 weeks after the birth on how to reduce exposure to mite, pet and food allergens, and passive smoking. The dietary recommendations were to breastfeed for ≥6 months and, if supplementation was necessary or if breastfeeding stopped before age 6 months, to use extensively hydrolysed formula milk and to postpone the introduction of solid foods until age 6 months.
During the first 2 years of life, the incidence of asthma-like symptoms was similar in both groups: however, subanalysis revealed a significant reduction in the female, but not the male intervention group. At age 2 years, the intervention group had fewer asthma symptoms, including wheezing, shortness of breath and night-time cough than the control group.
Feeding hypoallergenic formula or the introduction of solid foods at <6 months were not significantly associated with asthma symptoms at age 2 years or earlier but breastfeeding was significantly negatively correlated with wheezing at age 2 years or earlier.

One RCT (quality rating 1-) from Sweden and Finland (Odelram et al. 1996) compared the effectiveness of ultra-filtered cow's milk whey formula with standard cow's milk formula in preventing the development of atopy in infants at high risk (N=91). Infants of mothers receiving antenatal care were included if they had at least two atopic family members or one atopic parent and cord blood total IgE ≥0.5kU/l. The socio-economic background of the mothers was not reported. All mothers were advised to avoid cow's milk, egg and fish from 10 days before expected date of

delivery and throughout breastfeeding. They were also advised to breastfeed exclusively for at least 4 months, and not to give fish, egg or cow's milk products to their infants during the first 12 months of life. When weaning began infants in the intervention group received the ultra-filtered cow's milk whey formula and control group infants received standard cow's milk formula. Twenty infants were exclusively breastfed for 9 months or more, and were analysed as a separate group. At 18 months, among the 71 randomised infants who received formula, atopic disease had developed after the introduction of formula in 10/32 (31%) of the intervention group, and in 15/39 (39%) of the control group. These differences were not statistically significant, nor were those for skin prick tests or IgE levels.

A RCT (quality rating 1-) from Sweden (Oldaeus et al. 1997) examined the incidence and severity of atopic disease and allergic sensitisation during the first 18 months of life in infants at risk (N=155). Infants of pregnant women attending well mother clinics in three towns in southeast Sweden were included if they had at least two atopic family members, or one atopic family member and cord blood IgE concentration ≥0.5 kU/l. The socio-economic background of the mothers was not reported. All the mothers included in the study exclusively breastfed until their infants were weaned. All mothers were asked to eliminate cows' milk, eggs and fish from their diet from one week before the expected birth date until breastfeeding ended, and to exclude from their infants' diet: milk to age 9 months, eggs, fish and citrus fruits to age one year, and other solid foods to age 4 months. Infants were randomised when mothers decided to supplement breast milk with formula milk. They received either an extensively hydrolysed casein formula (N), a partially hydrolysed formula (whey: casein ratio, 60:40) (PH), or a routine cows' milk formula (RM) until 9 months of age. Significantly higher rates of wheezing were found in the RM group compared with the N group (p=0.031) during the first 18 months. Differences at 6, 9 and 12 months, and differences between N and PH group were not significant. Significantly higher rates of atopic dermatitis were found in the PH group (44%) (p=0.004) and RM group (41%) (p=0.006) than in the N group (17%) in the first 9 months. Inter-group differences were not found to be significant at 6, 12 or 18 months. Cumulative atopic symptoms were significantly less in the N group than in the RM group at 6, 9, 12 and 18 months (p=0.013 to <0.001). They were also significantly less in the N group than in the PH group at 6 months (p=0.025) and 9 months (p=0.018). Cumulative atopic symptoms were also significantly less in the PH group than in the RM group at 18 months (p=0.039). Significantly fewer in the N group (10%) than in the PH group (33%) had positive skin prick test for eggs at 9 months (p=0.006).

A RCT (quality rating 1-) from Germany (Von Berg et al. 2003) investigated the allergy-preventive effect of three differently hydrolyzed infant formulae compared with a conventional cow's milk formula (N=2252). Participants were healthy newborn infants with at least one family member (mother, father, or biologic sibling) with an allergic disease. All the mothers were advised to breastfeed exclusively for at least four months and preferably for six months. No dietary restrictions during lactation were recommended. The time of weaning and introduction of study formula was decided by the mothers. Mothers were asked not to feed solid food during the first 4 months and thereafter to add not more than one food per week and to avoid milk and dairy products, hen's eggs, soy products, fish, nuts, tomatoes and citrus fruits in the first year. At any point, if children received formula, they received one of the following (determined during randomisation at birth): conventional cow's milk formula; partially hydrolysed whey formula; extensively hydrolysed whey formula; or extensively hydrolysed casein formula. Children who were exclusively breastfed for four months or more were not included in the analysis (889 children, 39%). Only 945 children were included in the final analysis (reasons for dropout are discussed in

detail in the paper).  The incidence of allergic manifestation in the extensively hydrolysed casein formula group was found to be significantly reduced compared with that in the conventional cow's milk formula group (p=0.036).  The reduction in incidence of allergic manifestation found in the two whey hydrolysate groups was not statistically significant.  The authors reported that an intention to treat analysis which included all subjects with a 4 week follow-up (n=2138 (95%)), including those exclusively breastfed, confirmed the results given but they were less 'prominent'.

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*Strength and applicability of evidence*

Three RCTs (all 1-) examined the effectiveness of modified cow's milk formulae *and* dietary restriction to prevent atopy in children at high risk.
A trial conducted in Sweden and Finland (Odelram et al. 1996) found no differences between children given ultra-filtered cow's milk whey formula and those given standard cow's milk formula.
An under powered RCT in Sweden (Oldaeus et al. 1997) compared extensively hydrolysed casein formula, partially hydrolysed formula (whey: casein ratio, 60:40) and standard infant formula from the start of weaning to age 9 months in infants with a family history of atopy. Allergy preventive measures were also recommended including discouraging smoking and dietary exclusion of cow's milk, eggs, fish and citrus fruits in both mothers and infants diets. The study found extensively hydrolysed casein formula had a positive allergy-preventive effect during the first 18 months of life but not partially hydrolysed formula when compared to standard infant formula. Similarly, a German study (Von Berg et al. 2003) also reported more positive outcomes among children receiving an extensively hydrolysed casein formula compared to conventional cow's milk formula, however partially and extensively hydrolysed whey formulae were not effective.

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### 5.3.3  Subquestions

Table 1: Sub-questions for studies on allergies

| Reference | How does the structure and content of the intervention influence effectiveness? | Does effectiveness vary by gender, age, ethnicity, religious practices or social/ professional group of those receiving or delivering the intervention? | Does effectiveness vary with site/ setting or intensity/ duration of the intervention? | What are the views of those receiving and delivering the intervention? | Is there evidence of unintended or harmful effects? | Are there barriers to replication of effective interventions? |
|---|---|---|---|---|---|---|
| Kalliomaki et al. 2001 & Kalliomaki et al. 2003 | Some infants received the probiotic via breast milk and others were given the probiotic on a spoon. This made no | Not reported | Not reported | Not reported | No – other than allergic disorders | Modes of delivery and long time of administration of the probiotic may be barriers for some parents |

| Reference | How does the structure and content of the intervention influence effectiveness? | Does effectiveness vary by gender, age, ethnicity, religious practices or social/ professional group of those receiving or delivering the intervention? | Does effectiveness vary with site/ setting or intensity/ duration of the intervention? | What are the views of those receiving and delivering the intervention? | Is there evidence of unintended or harmful effects? | Are there barriers to replication of effective interventions? |
|---|---|---|---|---|---|---|
| Finland RCT 1+ | difference to the positive effect of the intervention | | | | | |
| Arshad et al. 1992 & Hide et al. 1994 & Hide et al. 1996 UK RCT 1+ | The differential effects of formula, food avoidance and house-mite avoidance cannot be separated | The authors did not examine the effects of the intervention by socio-economic group. They did however, examine the overall risks of developing allergic disorders by socio-economic group and found that infants in lower socio-economic groups have a significantly higher risk. | The authors state that a longer follow-up period is required to find out whether the reduction in allergic disorders would be maintained. | The authors state that passive smoking is an important risk factor that should be addressed in any prophylactic programme. | No – other than allergic disorders | As the authors note, a strict diet may be hard to follow. There would be costs involved in supplying polyvinyl-covers for mattresses and in supplying anti-dust-mite treatment. |
| Odelram et al. 1996 Sweden and Finland RCT 1- | The differential effects of formula and food avoidance cannot be separated | It is not clear whether age of infant at introduction of formula is a confounding factor | Not reported | See Barriers | No – other than allergic disorders | Authors note the difficulty of adhering to a strict dietary protocol and state many families with babies at high risk of |

| Reference | How does the structure and content of the intervention influence effectiveness? | Does effectiveness vary by gender, age, ethnicity, religious practices or social/ professional group of those receiving or delivering the intervention? | Does effectiveness vary with site/ setting or intensity/ duration of the intervention? | What are the views of those receiving and delivering the intervention? | Is there evidence of unintended or harmful effects? | Are there barriers to replication of effective interventions? |
|---|---|---|---|---|---|---|
| | | | | | | atopy found participation too demanding<br><br>Exclusive breastfeeding to 4 months and beyond is uncommon in the UK |
| Oldaeus et al. 1997<br><br>Sweden<br><br>RCT<br><br>1- | The differential effects of formula and food avoidance cannot be separated | Not reported | Not reported | Researchers note the study was under-powered | No – other than allergic disorders | A strict diet may be hard to follow |
| Schonberger et al. 2005<br><br>The Netherlands<br><br>RCT<br><br>1+ | Although the intervention was multifaceted with reduced exposure to mite allergens, food allergens and passive smoking, multiple logistic regression analysis showed that all three contributed independently of each other to asthma symptoms. | Asthma symptoms were significantly reduced in the intervention group for both boys and girls at age 2 years but only significantly for girls at age 0-2 years. | Not reported | Not reported | No – other than allergic disorders | The dust mite removal regime was extensive. Restriction of exposure to pet allergens may not be acceptable to all families. Encouragement for mother to stop smoking while pregnant and both parents to stop smoking for the first 2 years should be stressed. |
| Von Berg | The | Effectivenes | Effectivene | The | No – other | Authors note |

| Reference | How does the structure and content of the intervention influence effectiveness? | Does effectiveness vary by gender, age, ethnicity, religious practices or social/ professional group of those receiving or delivering the intervention? | Does effectiveness vary with site/ setting or intensity/ duration of the intervention? | What are the views of those receiving and delivering the intervention? | Is there evidence of unintended or harmful effects? | Are there barriers to replication of effective interventions? |
|---|---|---|---|---|---|---|
| et al. 2003<br><br>Germany<br><br>RCT<br><br>1- | differential effects of formula and food avoidance cannot be separated | s did not vary with nationality or parental education | ss did not vary by study centre<br><br>Intention to treat analysis is not presented, results are for those who received the intervention as per protocol | formula shown to be effective (extensively hydrolysed casein formula) had the worst compliance rate<br><br>Authors state due to its processing this formula tasted and smelt worse than the others, and suggest this is why some mothers and babies rejected it | than allergic disorders | the study protocol was demanding for the mothers<br><br>Exclusive breastfeeding to 4 months and beyond is uncommon in the UK |

The search did not identify any UK studies that would provide corroborative evidence.


## 5.4   Key question 4

*What dietary interventions help prevent diet-related dental caries in infants and young children?*

Two SRs were identified that were relevant to this question (Holm et al. 2002 (2-), SIGN 2005 (2+)). The first was an English language summary of a Swedish SR (Holm et al 2002) (quality rating 2-) that examined the effectiveness of various interventions on caries prevention. This review largely focussed on fluoride, but some

dietary interventions were also examined. The review identified no studies on the effects of dietary information (i.e. reducing sugar consumption and the frequency of intake) on preventing caries. Insufficient evidence was found to determine whether sugar substitutes (sorbitol and xylitol) in chewing gum and sweets have any preventive effects on caries. The review graded evidence from 1 to 4, i.e. from strong to insufficient scientific support, and therefore the dietary interventions that were identified provided the lowest level of evidence. (Further information was not available in the summary.)

The second review was SIGN (2005) which was a recently published (November 2005) national clinical guideline conducted by the Scottish Intercollegiate Guidelines Network (SIGN) and therefore directly applicable to the UK. This guideline incorporated an extensive search of the literature, and presents levels of evidence from 1++ to 4 (the latter being "expert opinion") and grades of recommendations as guidelines from A to C. Guidelines were not specifically aimed at particular age groups. In this document there is a chapter covering diet and nutrition in which two sections contained study results relevant to this review: "Milk feeding and caries" and "Free sugars and dental caries". Limited data were reported from the individual studies, but have been summarised as follows[1]. Relevant studies of children aged 2-5 years are included in the NICE review for 2-5 year-old children and were from three sections of the SIGN review: "Free sugars and dental caries", "Other foodstuffs and caries" and "Sugar substitutes".

### 5.4.1  Milk feeding and caries

Much of the research examining cariogenicity of milk feeds is laboratory based.

- A SR of epidemiological studies found inconsistent evidence of an association between breastfeeding beyond one year and the development of early caries (Valaitis et al, 2000) (graded 2+ by SIGN reviewers). The review included 28 studies: 24 case-control studies, three case-series and one cross-sectional study. Studies were graded for quality as strong/moderate/weak/very weak: the majority were graded weak (32%) or very weak (57%), only three studies were of moderate quality and there were none of strong quality.  Conclusions were based only on the results from the twelve moderate and weak studies.

- A SR (Reisine and Psoter 2001) (graded 2+ by SIGN reviewers) evaluated the association between the incidence and prevalence of dental caries and the use of a baby bottle (specifically past the age of 12 months). The relevant publication concentrated on the association between socio-economic status and dental caries. The authors (Reisine and Psoter) commented that the literature was weak and more detail of feeding practices was required e.g. use of a bottle at bedtime or a description of bottle contents.  Duration of bottle use in itself was not significantly associated with caries risk, but sweetened milk or juice given in a bottle increased the risk of caries.

Relevant SIGN guidelines: Members of the dental team should support and promote breastfeeding according to current recommendations (grade C). Parents and carers should be advised that drinks containing free sugars, including natural fruit juice, should never be put in a feeding bottle (grade C).

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[1] Of the studies included in the guideline, only those which may be applicable to young children have been summarised in this rapid review. The guidelines included additional recommendations based on the clinical experience of the guideline development group. These have not been summarised in this rapid review.

### 5.4.2  Free sugars in food/ fluids

- A US prospective study of children from low-income families (N=122) attending a nutrient supplement programme aged 6-24 months (graded 3 by SIGN reviewers) reported a high risk of mutans streptococci (MS) colonisation associated with having sweetened bottle contents (Mohan et al. 1998). Twenty per cent of children under 14 months of age were colonised with MS, including four of 22 infants aged 6-9 months, indicating that colonisation may begin earlier than in some investigations. Children whose bottles contained sweetened beverages were more likely to be colonised than children whose bottles contained milk.

- A large cross-sectional study of Australian children aged 4-6 years (graded 3 by SIGN reviewers) found an increased risk of caries at age <6 years associated with sweetened bottle content, sleeping with a bottle and sipping from the bottle during the day (Hallett 2002).  (This study is relevant to the NICE review for 2-5 year-old children, which contains more details.)

Relevant SIGN guidelines: Parents and carers should be advised that drinks containing free sugars, including natural fruit juices, should be avoided between meals. Water or milk may be given instead (grade C).

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*Strength and applicability of evidence*

A recently published UK guideline (SIGN 2005) (2+) includes two relevant SRs (graded 2+ by reviewers).

One SR (Valaitis et al 2000, graded 2+ by reviewers) of epidemiological studies found no consistent high quality evidence of an association between breastfeeding beyond one year and the development of early dental caries.

Another SR (Reisine and Psoter 2001, graded 2+ by reviewers) based on poor quality studies found evidence that the duration of bottle use (specifically beyond age 12 months) was not related to caries risk but weak evidence that sweetened milk or juice in a bottle increased the risk of early childhood caries (at age <6 years).

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### 5.4.3  Corroborative UK evidence

**Blinkhorn and Davies, 1999**

Health visitors in Salford, a socio-economically deprived area, worked with the community dental service to devise a dental package that contained a feeder cup, baby toothpaste and brush, and dental literature highlighting the importance of the early use of a feeder cup instead of a bottle, as well as 'safe' drinks (sic) to give the baby.  Another leaflet was included which stressed the importance of registering the baby with a dentist and the use of sugar-free medicine.

From May 1997 the pack was given to mothers at the 8-month check.  The 8-month check was chosen because it included an important hearing test and virtually all mothers and babies were seen by a health visitor at this stage.  Eight months was also the age being advised for mothers to wean their babies off the bottle and on to a feeder cup.

Mothers of 250 babies who had recently received the 8-month check were sent a postal questionnaire in November 1996 that asked if they recalled receiving items of advice at the check. The same questionnaire was sent to 250 mothers in November 1997. Response rates were 170/250 (68%) and 182/250 (79%) respectively. The percentage of responders saying 'yes' to each item before and after the intervention were as follows: use of a feeder cup (54% before, 93% after); tooth brushing with fluoride toothpaste (44% before, 84% after); restricting sugary foods and drinks (62% before, 91% after); using sugar-free medicines (38% before, 71% after) registration with a dentist (47% before, 745 after). All these differences were found to be statistically significant (p<0.001).

The authors were aiming to discover whether this improvement in mothers' knowledge was matched by health gains in their children, by collecting data from dental examinations of the children involved in this programme at age 3 years.


## 5.5   Key question 5

*What interventions effectively help mothers continue breastfeeding after 6 months, both at home and out of the home, for example, during return to paid employment?*

Jones 2004 (quality rating 1-) reported on a UK pilot study that aimed to support continued breastfeeding for mothers who plan to return to work. Pregnant women who intended to breastfeed and planned to continue to breastfeed after returning to paid employment were recruited during pregnancy, from community settings in two areas of Staffordshire (N=75). No socio-economic information about the mothers was reported. The intervention was a one-hour evidence-based session of specialist lactation advice from the researcher. A session was arranged with each woman who confirmed, some weeks after the birth that she was breastfeeding and she still planned to return to work. The advice covered principles and technique of milk expression, handling and storage of expressed milk and management of milk supply, and was reinforced by a written leaflet. The control group received standard care from community midwives and health visitors, in which advice on breastfeeding and returning to work was ad hoc. Intervention and control groups were numerically unbalanced and follow-up was generally low (29/75, 39%). No statistically significant differences between the groups were found between numbers of women who expressed milk at work or infants exclusively fed expressed breast milk while their mothers were working, except that 12/19 women in the intervention group, compared with 5/10 controls, practised milk expression prior to returning to work (p=0.04).

### 5.5.1 Subquestions

Table 2: Sub-questions for studies promoting breastfeeding for 6 months or more

| Reference | How does the structure and content of the intervention influence effectiveness? | Does effectiveness vary by gender, age, ethnicity, religious practices or social/ professional group of those receiving or delivering the intervention? | Does effectiveness vary with site/ setting or intensity/ duration of the intervention? | What are the views of those receiving and delivering the intervention? | Is there evidence of unintended or harmful effects? | Are there barriers to replication of effective interventions? |
|---|---|---|---|---|---|---|
| Jones et al. 2004 UK RCT 1- | Pilot study, meant to test trial methods rather than demonstrate effectiveness of the intervention | Not reported | Many women found barriers to expressing milk at work impossible to overcome | Some women reported that practising expressing their milk was helpful | None apparent | N/A |

### 5.5.2 Corroborative UK evidence

The search identified two UK studies that provided corroborative evidence of support for breastfeeding beyond 6 months.

**Bolling et al. 2007**
Relevant details are given in Section 5.1 Key question 1.

**Fulton et al. 1998**

Participants were breastfeeding women who attended a fortnightly breastfeeding support group set up by health visitors in a community centre used by a variety of groups of women in this Urban Aid-designated Area of Deprivation. At the meetings, experiences were shared informally over coffee, followed by a discussion of a predefined topic. Two health visitors attended. A crèche worker cared for older children in an adjacent area.

Control data from an audit of every breastfed baby born in the area during 1996 gave an initiation of breastfeeding rate of 25% and, among this 25%, duration of breastfeeding 6 months or more for 26%. Approximately 12% of the area's breastfeeding mothers used the support group. Among the support group users, 59% continued to breastfeed for longer than 6 months.

The authors state that the audit demonstrated the need to examine current breastfeeding practice at the local hospital especially time of first feed and administration of extra fluids. They consider their decision to concentrate their limited professional resources in the group enabled those women already committed to breastfeeding to succeed, and that success in overcoming practical and cultural barriers to breastfeeding enhanced these women's self-esteem.

**Hoddinott et al. 2006**

Participants were staff and mothers (including expectant mothers) attending breastfeeding support groups in four rural postcode areas of north-east Scotland with a socio-economically mixed population and low breastfeeding rates.  The intervention used action research methodology, so that feedback from group members resulted in within-group and between-group variation in group structure and content; one precisely defined, reproducible model did not suit all areas.  Breastfeeding data for the study area were collected for 9 months baseline before the intervention and 9 intervention months.  After the intervention, both exclusive breastfeeding and any breastfeeding increased at all time points to 8 months.  The increases were not statistically significant after 2 weeks (p=0.016 at birth, p=0.001 at hospital discharge, p=0.012 at 1 week, p=0.017 at 2 weeks, p=0.129 at 6 weeks, p=0.055 at 4 months, p=0.096 at 8 months).  Outcomes varied by place of birth (mothers giving birth at a midwife-led unit within the area breastfed longer than mothers giving birth at a district general hospital outside the area) and by group (areas with lowest baseline breastfeeding rates had the largest increases, whereas in the area with the highest baseline rates, breastfeeding declined).
The researchers state that the action research model was highly valued, particularly by breastfeeding group facilitators, and has enabled the intervention to make the transition smoothly from research into routine practice without need for additional resources.

**Kosmala-Anderson et al. 2006**

The UK cross-sectional study of breastfeeding support at work (Kosmala-Anderson et al. 2006) was of both male and female employees (N=46) in Coventry who were: either planning to go on maternity leave with the next 6 months (n=1, one woman), or on maternity leave (n=31 of the 44 women (70.5%)) or within 6 months of returning from maternity leave (n=12). There were 2 male participants. The predominately white subjects (median age in the range 30-35 years, 61% educated after age 18 years) were employed in four large public sector organisations: Coventry Council, South Warwickshire PCT, Coventry University and South Warwickshire General Hospitals NHS Trust. Almost 80% of women wanted to continue breastfeeding after returning to work. Ninety per cent of respondents were not aware of any employer policy nor offered any relevant information concerning available support, despite two organisations having a range of breastfeeding-related policies in development and some facilities in place. Almost 90% of respondents stated that employers should do more to support breastfeeding, which should include: access to facilities to express and store breast milk; to enable them to work flexible hours; and to enable them to take rest breaks during working hours. The authors additionally suggested that mothers should have the opportunity to breastfeed their babies at local childcare facilities.

The authors compared US, Australian, European and UK legislation regarding support for breastfeeding after returning to work and reviewed relevant research regarding the relationship between breastfeeding support at work and duration of breastfeeding, identifying three relevant US work intervention studies (Cohen & Mrtek 1994, Cohen et al. 2002 and Ortiz et al. 2004) and two cross-sectional studies in Spain (Escriba et al. 1994) and the US (Rischel & Sweeney 2005). Two of the US intervention studies provided relevant data for breastfeeding beyond age 6 months. A Fathering Programme of male employees in Los Angeles offered fathers (N=128) and their partners breastfeeding education classes, including full individual lactation counselling for both parents and breast pumps to use at home and at work (Cohen et

al. 2002). Sixty six per cent of female partners were employed either full-time or part-time. Infants of the participating fathers were breastfed for an average of 8 months and 69% infants were still breastfed at age 6 months. The second study used retrospective records of women employed in five US corporations (N=462) of a lactation programme with a choice of: a class on the benefits of breastfeeding; access to a lactation councillor by visit and phone call in pregnancy and throughout return to work while breastfeeding; and facilities and equipment to pump at work (Ortiz et al. 2004). Breastfeeding was initiated by 97.5% women and 57.8% continued for ≥6 months. Of the 435 women (94.2%) who returned to work, 343 women (78.9%) attempted using a breast pump at work, of which 98% were successful at expressing milk in the workplace for a mean 6.3 months. Mean postnatal maternity leave was 2.8 months. Women who were salaried were more likely to use a breast pump at work than those who were paid hourly wages, $p<0.01$.

# 6 Overview and Discussion

Weaning is an important time in the life of a family, when healthier eating patterns can be established. Regrettably, there is an overall paucity of high quality intervention studies concerning safe and healthy feeding practices for infants and young children who are no longer predominantly milk fed.

In a SR by Elkan et al. (2000), the authors concluded that there was insufficient evidence regarding the impact of home visiting on children's diet. However, this SR included studies on disadvantaged and low income families in the US and the Republic of Ireland, in which it appears that home visiting has had some success. This may warrant further investigation of the study components and their outcomes, so that similar programmes may be piloted in the UK. A SR by Tedstone et al. (1998) that included studies of disadvantaged and ethnic minority families in the UK concluded that there was insufficient evidence to make recommendations about optimum weaning and post-weaning dietary practices. Tedstone et al. (1998) made specific recommendations for research, namely:

"Research on the promotion of optimal weaning and post-weaning feeding practices in the UK should focus on

- developing effective promotional programmes on optimal weaning practices for the UK setting
- interventions that specifically delay to 4 months of age (sic) the introduction of solids, increase the intake and availability of iron, reduce the use of unmodified cow's milk, reduce the use of non-milk extrinsic sugars and increase the variety of weaning foods, and
- those at greatest risk of developing nutritionally related health problems such as iron deficiency, anaemia and dental caries".

In relation to the third of these points, diet may not be the only factor that affects anaemia in young children. For example, populations of young children may include some with undiagnosed haemoglobinopathies.

No studies addressed the promotion of uptake of recommended vitamin and micronutrient supplements. This demonstrates a need for such promotional studies.

There were a number of studies that addressed food allergies and intolerance. Based on one good quality study, it appears that the use of probiotics may be beneficial to reduce atopic eczema, but further research is necessary to substantiate these findings.

The recent comprehensive review by Osborn and Sinn (2006) found that early supplementary feeding or sole feeding with hydrolysed formula for the first few days did not reduce the risk of allergy when compared to exclusive breastfeeding (2 studies). The SR also provided evidence to support feeding high risk infants who can not be exclusively breastfed hydrolysed formula in stead of cow's milk formula for the first few months in order to prevent infant allergy (7 studies). The majority of the studies used for the meta-analysis used partially hydrolysed formula and similarly partially hydrolysed whey formula as opposed to partially hydrolysed casein formula. Meta-analysis was only possible for three studies of extensively hydrolysed formula compared to cow's milk formula used in the first few months, which also found a significant decrease in infant allergy but the analysis was dominated by one study. Meta-analysis for a comparison of extensively hydrolysed formula versus partially

hydrolysed formula in the first few months found a significant reduction in infant allergy but was only possible for three studies. There is a need for more well-conducted RCTs comparing extensively hydrolysed formula, partially hydrolysed formula and cow's milk formula.

The studies on formula appear to demonstrate a trend towards less atopic disease with more extensively hydrolysed casein formula, but they examined differently modified formulae and used different co-interventions. Influential work by Chandra on infant formula has recently been discredited[2]. Until now, Chandra's work has been very influential in people's thinking about the use of specific formula preparations. Another relevant factor is that extensively hydrolysed formula has a less acceptable taste to that of partially hydrolysed formula. It is also noted that the probiotics and formula/allergenic food trials were all funded by infant formula manufacturers. Again, further research is necessary before any recommendations could be made. When recommendations are made, they need to be made cautiously for the population as a whole. In addition, there is a need for consistent advice in this area from health care professionals.

A guideline recently published in Scotland (SIGN 2005) has presented a number of useful recommendations on dental health promotion which could be adopted in the rest of the UK. The main issues to highlight from this work is the lack of evidence that extended breastfeeding causes tooth decay. Consideration should also be made when feeding from a bottle to the types of drinks consumed and length of time teeth are exposed to sweet drinks.

There was a lack of good quality evidence from interventions specifically aimed at supporting breastfeeding after six months in women who planned to return to paid employment. A lack of effective support for breastfeeding after 6 months raises wider questions of culture and policy. Effective support for breastfeeding should include facilitating breastfeeding in public and addressing the problems of women's employment and breastfeeding. Breast milk is an important component of a child's life, and should certainly be seen as such up to at least age 2 years (WHO 2003[3]). Children receiving breast milk for longer would reduce the need for other (sugar containing) drinks, but will require a cultural shift in both the home and the workplace.

Overall, there are important gaps in the evidence base – for example, no studies have addressed the practical problems of weaning, which include choosing and preparing appropriate foods, behavioural problems in the child, including food refusal, and tiredness in the mother. There is a paucity of information on follow-on formula milks, which are widely available and widely used. There are questions about their nutritional adequacy, and also about their marketing to parents. No studies have looked at the use of bottles/ cups/ spoons as ways of feeding fluids to older babies. None have investigated what may be the best strategies either to assist mothers to wean successfully (i.e. good range of appropriate foods, happy child etc) or to encourage children and families to eat a wide range of healthy foods, and resist unhealthy foods. Again, such unhealthy foods are easily accessible, and attractively and aggressively marketed to very young children and parents.

More integration of topic areas is needed across dental, nutritional, health visiting/midwifery, and other evidence bases. Researchers and families need to be aware of the whole range of available evidence from a spectrum of disciplines.

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[2] http://www.babymilkaction.org/press/press3feb06.html
[3] http://www.waba.org.my/docs/gs_iycf.pdf

# 7  Additional References

**Studies within included reviews**

Barker, W. and R. Anderson (1988). "The Child Development Programme: an evaluation of process and outcome." Bristol, Early Childhood Development Unit, University of Bristol.

Barker, W., R. Anderson, et al. (1994). "Health trends over time and major outcomes of the Child Development Programme." Bristol, Early Child Development Unit, University of Bristol and Eastern Health and Social Services Board.

Burt, B. and S. Pai (2001). "Sugar consumption and caries risk: a systematic review." School of Public Health, University of Michigan, Ann Arbor, MI, USA. **2006**.

Childs, F., A. Aukett, et al. (1997). "Dietary education and iron deficiency anaemia in the inner city." Archives of Diseases in Childhood **76**(2): 1447.

Chirico, G., A. Gasparini, et al. (1997). "Immunogenicity and antigenicity of a partially hydrolysed cow's milk infant formula." Allergy **52**: 82-8.

De Seta, L., P. Siani, et al. (1994). "The prevention of allergic diseases with a hypoallergenic formula: a follow-up at 24 months. The preliminary results." La Pediatria Medica e Chirurgica: Medical and Surgical Pediatrics." **16**: 251-4.

Frank, D. A., S. J. Wirts, et al. (1987). "Commercial discharge packs and breastfeeding counseling: effects on infant-feeding practices in a randomized trial." Pediatrics **80**(6): 845-54.

Gedalia, I., S. Ben-Mosheh, et al. (1994). "Dental caries protection from hard cheese consumption." American Journal of Dentistry **7**(6): 331-2.

Griffiths, B., M. Poynor, et al. (1995). "Health education and iron intake of weaning children." Health Visitor **68**(10): 418-9.

Gutelius, M. F., A. D. Kirsch, et al. (1977). "Controlled study of child health supervision: behaviour results." Pediatrics **60**: 294-304.

Halken, S., K.S. Hansen, et al. (2000). Comparison of a partially hydrolysed infant formula with two extensively hydrolysed formulas for allergy prevention: a prospective, randomised study." Pediatric Allergy and Immunology 11: 149-61.

Hallett, K. and P. K. O'Rourke (2002). "Earlu childhood caries and infant feeding practice." Community Dent Health **19**: 237-42.

Johnson, Z., F. Howell, et al. (1993). "Community mothers' programme: randomised controlled trial of non-professional intervention in parenting." British Medical Journal **306**(6890): 1449-52.

Juvonen, P., M. Mansson, et al. (1996). "Allergy development and macromolecular absorption in infants with different feeding regimens during the first three days of life. A three-year prospective follow-up." Acta Paediatrica **85**: 1047-52.

Karjalainen, S., Y. Le Bell, et al. (1988). "Salivary parameters and efficiency of dietary instructions to reduce sugar intake among 7-8 year-old schoolchildren." Scandinavian Journal of Dental Research **90**: 22-9.

Lam, B.C.C., C.Y. Yeung, et al. (1992). "The effect of breast milk, infant formula and hypoallergenic formula on incidence of atopic manifestation in high risk infants." Nestlé Internal Report. *(unpublished data only)*

Lapinleimu, H., J. Viikari, et al. (1995). "Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol." Lancet **345**(8948): 471-6.

Lingstrom, P., A. K. Holm, et al. (2003). "Dietary factors in the prevention of dental caries: a systematic review." Acta Odontol Scand **61**(6): 331-40.

Mackie, I. C., H. V. Worthington, et al. (1983). "An investigation into sugar-containing and sugar-free over-the-counter medicines stocked and recommended by pharmacists in the North Western Region of England." British Dental Journal **175**: 93-8.

Maggio, L., A.A. Zuppa, et al. (2005). "Higher urinary excretion of essential amino acids in preterm infants fed protein hydrolysates." Acta Paediatrica **94**: 75-84.

Mallet, E., A. Hencocq, et al. (1992). "Long-term prevention of allergic diseases by using protein hydrolysate formula in at-risk infants." Journal of Pediatrics **121**: S95-100.

Marini, A., M. Agosti, et al. (1996). "Effects of a dietary and environmental prevention programme on the incidence of allergic symptoms in high atopic risk infants: three years' follow-up." Acta Paediatrica (Suppl) **414**: 1-21.

Marshall, T. A., S. M. Levy, et al. (2003). "Dental caries and beverage consumption in young children." Pediatrics **112**(3pt1): e184-91.

McEnery, G. and K. P. Rao (1986). "The effectiveness of antenatal education of Pakistani and Indian women living in this country." Child: Care, Health and Development **12**(6): 385-99.

Mohan, A., D. E. Morse, et al. (1998). "The relationship between bottle useage/content, age, and number of teeth with mutans streptococci colonisation in 6-24 month old children." Community Dent Oral Epidemiol **26**(1): 12-20.

Nentwich, I., E. Michkova., et al. (2001). "Cow's milk specific cellular and humoral immune responses and atopy skin symptoms in infants from atopic families fed a partially (pHF) or extensively (eHF) hydrolysed infant formula." Allergy **56**: 1144-56.

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Reisine, S. T. and W. Psoter (2001). "Socioeconomic status and selected behavioural determinants as risk factors for dental caries." J Dent Educ **65**(10): 1009-16.

Rodrigues, C. S. and A. Sheiham (2000). "The relationships between dietary guidelines, sugar intake and caries in primary teeth in low-income Brazilian three-year-olds: a longitudinal study." International J Paediatric Dent **10**(1): 47-55.

Saarinen, K.M., K. Juntenen-Backman, et al. (1999). Supplementary feeding in maternity hospitals and the risk of cow's milk allergy: A prospective study of 6209 infants." Journal of Allergy and Clinical Immunology **104**: 457-61.

Sakai, O. and K.-I. Horii (1980). "Spreading the effect of caries prevention by community organisation in schoolchildren in Japan." Journal of Dental Research **59**: 2226-32.

Szajewska, H., P. Albrecht. et al. (2001). "Extensive and partial protein hydrolysate preterm formulas: the effect on growth rate, protein metabolism indices, and plasma amino acid concentrations." Journal of Pediatric Gastroenterology and Nutrition **32**: 303-9.

Tsai, Y.T., C.C.Chou, et al. "The effect of hypoallergenic formula on the occurrence of allergic diseases in high risk infants." Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi **32**: 137-44.

Valaitis, R., R. Hesch, et al. (2000). "A systematic review of the relationship between breastfeeding and early childhood caries." Can J Publ Health **91**(6): 411-7.

Vandenplas, Y., B. Hauser, et al. (1992) "Effect of a whey hydrolysate prophylaxis of atopic disease." Annals of Allergy **68**: 419-24.

Vandenplas, Y., B. Hauser, et al. (1993) "The nutritional value of a whey hydrolysate formula compared with a whey-predominant formula in healthy infants." Journal of Pediatric Gastroenterology and Nutrition **17**: 92-6.

Willems, R., J. Duchateau, et al. (1993). "Influence of hypoallergenic milk formula on the incidence of early allergic manifestations in infants predisposed to atopic diseases." Annals of Allergy **71**: 147-50.

**UK studies**

Anderson A.S., C.-A. Guthrie, et al. (2001) "Rattling the plate – reasons and rationales for early weaning." <u>Health Education Research</u> **16**(4): 471-9.

Alder E.M., F.L.R. Williams, et al. (2004) "What influences the timing of the introduction of solid food to infants?" <u>British Journal of Nutrition</u> **92**: 527-31.

Blinkhorn, F. and Davis, K (1999). "Reducing nursing caries: the role of health visitors." <u>Community practitioner</u> **72**(6): 174-5.

Bolling, K., C. Grant C, et al. (2007) <u>"Infant Feeding Survey 2005."</u>  London: The Information Centre, Government Statistical Service, UK Health Departments.

Cleghorn, S. (2006) "<u>Journal of Human Nutrition and Dietetics</u> **19**: 203-8.

Fulton, C., Kentley, L. et al. (1998). "Breastfeeding support: in a deprived area." <u>Community practitioner</u> **71**(5): 172-4.

Hoare K, Wright CM, Wilson P, Weaver LT (2002) Disseminating weaning messages: an intervention trial. <u>British Journal of Community Nursing</u> **7**(4): 196-200.

Hoddinott, P., Lee, A.J. et al. (2006). "Effectiveness of a Breastfeeding Peer Coaching Intervention in Rural Scotland." <u>Birth</u> **33**(1): 27-36.

Kosmala-Anderson, J., L.M. Wallace (2006). "Breastfeeding works: the role of employers in supporting women who wish to breastfeed and work in four organisations in England." <u>Journal of Public Health</u> **28**(3): 183-91.

Sritharan, N. and Morgan, J (2002). "Infant meal planners: A risk or remedy to the health of infants?" <u>Nutrition Bulletin</u> **27**(4): 241-242.

**References within UK studies**

Cohen, R., L. Lange, et al. (2002). "A description of male-focused breastfeeding promotion corporate lactation program." <u>Journal of Human Lactation</u> **18**(1): 61-5.

Cohen, R. and M.B. Myrtek (1994) "The impact of two corporate lactation programs on the incidence and duration of breastfeeding by employed mothers." <u>American Journal of Health Promotion</u> **8**: 436-51.

Escriba, V., C. Colomer, et al. (1994) "Work conditions and the decision to breastfeed in Spain." <u>Health Promotion International</u> **9**(4): 251-8.

Ortiz, J., K. Mcgilligan, et al. (2004). "Duration of breastmilk expression among working mothers enrolled in an employer-sponsored lactation program." <u>Pediatric Nursing</u> **30**(2): 111-9.

Richel, P.E.N. and P. Sweeney (2005) "Comparison of breastfeeding rates among women delivering infants in military treatment facilities with and without lactation consultants." <u>Military Medicine</u> **170**(5): 435-6.

# APPENDIX A – Included studies

**Systematic Reviews**

Elkan R, Kendrick D, Hewitt M, et al. (2000) The effectiveness of domiciliary health visiting: a systematic review of international studies and a selective review of the British literature. Health Technology Assessment. **4** (13):1-339.

Holm AK, Axelsson S, Dahlgren H, et al. (2002) Prevention of dental caries. Stockholm: Swedish Council on Technology Assessment in Health Care (SBU).

Osborn DA & Sinn J.  (2006) Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants. Cochrane Database of Systematic Reviews 2006, Issue 4. Art.No.:CD003664. DOI: 10.1002/14651858.CD003664.pub3.

SIGN. Prevention and management of dental decay in the pre-school child. In: Guideline no.83: SIGN; 2005. p. 44.

Tedstone A, Dunce N, Aviles M, Shetty PS. (1998) Effectiveness of interventions to promote healthy feeding in infants under one year of age. London: Health Education Authority.

**Randomised Controlled Trials (10 papers, 7 studies**)

Arshad SH, Matthews S, Gant C, et al. (1992) Effect of allergen avoidance on development of allergic disorders in infancy.[see comment]. Lancet. **339** (8808):1493-7.

Hide DW, Matthews S, Matthews L, et al. (1994) Effect of allergen avoidance in infancy on allergic manifestations at age two years. Journal of Allergy & Clinical Immunology. **93** (5):842-846.

Hide DW, Matthews S, Tariq S, Arshad SH (1996) Allergen avoidance in infancy and allergy at 4 years of age. Allergy. **51**(2): 89-93.

Jones E. (2004) Breastfeeding and returning to work. Practising Midwife. **7** (11):17-18, 20, 22.

Kalliomaki M, Salminen S, Poussa T, et al. (2003) Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial.[see comment]. Lancet. **361** (9372):1869-71.

Kalliomaki M, Salminen, S., Arvilommi, H. et al (2001) Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. Lancet. **357** (9):9262.

Odelram H, Vanto T, Jacobsen L, et al. (1996) Whey hydrolysate compared with cow's milk-based formula for weaning at about 6 months of age in high allergy-risk infants: effects on atopic disease and sensitization. Allergy. **51** (3):192-5.

Oldaeus G, Anjou K, Bjorksten B, et al. (1997) Extensively and partially hydrolysed infant formulas for allergy prophylaxis. Archives of Disease in Childhood. **77** (1):4-10.

Schonberger HJAM, Dompeling E, et al.  (2005) The PreVASC study: the clinical effect of a mulifaceted educational intervention to prevent childhood asthma. European Respiratory Journal. **25**: 660-670.

Von Berg A, Koletzko S, Grubl A, et al. (2003) The effect of hydrolyzed cow's milk formula for allergy prevention in the first year of life: The German Infant Nutritional Intervention Study, a randomized double-blind trial. Journal of Allergy & Clinical Immunology. **111** (3):533-540.

# APPENDIX B – Excluded studies

## Excluded SRs

| Paper - Systematic Reviews | Reason for Exclusion |
|---|---|
| AHRQ (2005) Effects of Omega-3 Fatty Acids on Child and Maternal Health. In: AHRQ Evidence Report no.118. | Not promotion of supplementation |
| Anderson JW, Johnstone BM, Cook-Newell ME (1995) Meta-analysis of the effects of soy protein intake on serum lipids. New England Journal of Medicine. 333 (5):276-282. | Sick children |
| Angermayr LCC (2004) Iodine supplementation for preventing iodine deficiency disorders in children. In: The Cochrane Database of Systematic Reviews: Reviews 2004 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003819.pub2. | Not promotion of supplementation |
| Baumgartner M, Brown CA, Exl BM et al. (1998) Controlled trials investigating the use of one partially hydrolyzed whey formula for dietary prevention of atopic manifestations until 60 months of age: an overview using meta-analytical techniques. Nutrition Research. 18 (8):1425-1442. | Not the most recent review on this topic, includes study by Chandra (work discredited) |
| Berry D, Sheehan R, Heschel R et al. (2004) Family-based interventions for childhood obesity: a review. Journal of Family Nursing. 10 (4):429-449. | Obesity |
| Bick D (1999) The benefits of breastfeeding for the infant. British Journal of Midwifery. 7 (5):312-319. | Not a review of interventions |
| Brown KH, Peerson JM, Rivera J et al. (2002) Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: a meta-analysis of randomized controlled trials. American Journal of Clinical Nutrition. 75 (6):1062-1071. | Children older than 5 years |
| Brunton G, Harden A, Rees R et al. (2003) Children and physical activity: a systematic review of barriers and facilitators.101. | Not diet |
| Butryn ML, Wadden TA (2005) Treatment of overweight in children and adolescents: does dieting increase the risk of eating disorders. International Journal of Eating Disorders. 37 (4):285-293. | Obesity |
| Cairns PA, Stalker DJ (2000) Carnitine supplementation of parenterally fed neonates. In: The Cochrane Database of Systematic Reviews: Reviews 2000 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000950. | Sick children |
| Callaghan A, Kendall G, Lock C et al. (2005) Association between pacifier use and breast-feeding, sudden infant death syndrome, infection and dental malocclusion. International Journal of Evidence-Based Healthcare. 3 (6):147-167. | Not diet |
| Campbell K, Waters E, O'Meara S et al. (2001) Interventions for preventing obesity in childhood: a systematic review. Obesity Reviews. 2 (3):149-157. | Obesity |
| Carroll AE, Garrison MM, Christakis DA (2002) A systematic review of nonpharmacological and nonsurgical therapies for gastroesophageal reflux in infants. Archives of Pediatrics and Adolescent Medicine. 156 (2):109-113. | Sick children |
| Ciliska D, Miles E, O'Brien MA et al. (1999) The effectiveness of community interventions to increase fruit and vegetable consumption in people four years of age and older. Ontario: Public Health Research Education and Development Program, Effective Public Health Practice Project, 45 (March). | Children older than 24 months |
| Collins CT, Makrides M, McPhee AJ (2006) Early discharge with home support of gavage feeding for stable preterm infants who have | Preterm infants |

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|---|---|
| not established full oral feeds. Collins CT, Makrides M, McPhee AJ. Early discharge with home support of gavage feeding for stable preterm infants who have not established full oral feeds (Cochrane Review). In: The Cochrane Library, Issue 1, Chichester, UK: John Wiley & Sons, Ltd. | |
| Contento I, Balch GI, Bronner YL et al. (1995) The effectiveness of nutrition education and implications for nutrition education policy, programs, and research: a review of research. Journal of Nutrition Education. 27 (6):277-418. | Children older than 24 months |
| Craig WR, Hanlon-Dearman A, Sinclair C et al. (2004) Metoclopramide, thickened feedings, and positioning for gastro-oesophageal reflux in children under two years. In: The Cochrane Database of Systematic Reviews: Reviews 2004 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003502.pub2. | Sick children |
| Eysenbach G, Powell J, Englesakis M et al. (2004) Health related virtual communities and electronic support groups: systematic review of the effects of online peer to peer interactions. British Medical Journal.1166-1170. | No studies on diets of young children |
| Gepkens A, Gunning-Schepers LJ (1996) Interventions to reduce socioeconomic health differences: a review of the international literature. European Journal of Public Health. 6 (3):218-226. | Not diet |
| Gera T, Sachdev HP (2002) Effect of iron supplementation on incidence of infectious illness in children: systematic review. British Medical Journal.1142-1144. | Not promotion of supplementation |
| Grotto I, Mimouni M, Gdalevich M et al. (2003) Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis. Journal of Pediatrics. 142 (3):297-304. | Not promotion of supplementation |
| Henderson G, Fahey T, McGuire W (2005) Calorie and protein-enriched formula versus standard term formula for improving growth and development in preterm or low birth weight infants following hospital discharge. In: The Cochrane Database of Systematic Reviews: Reviews 2005 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD004696.pub2. | Preterm infants |
| Ibrahim M, Sinn J, McGuire W (2006) Iodine supplementation for the prevention of mortality and adverse neurodevelopmental outcomes in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2006 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD005253.pub2. | Preterm infants |
| Institute for Clinical Systems Improvement (2005) Treatment of obesity in children and adolescents. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI).28. | Obesity |
| Kay, E.J. and Locker, D. (1997) Effectiveness of oral health promotion: a review. London, Health Education Authority<br><br>Kay, E.J. and Locker, D. (1998) A systematic review of the effectiveness of health promotion aimed at improving oral health. Community Dental Health 15 (3): 132-144 | Excluded after consultation with NICE. Most included studies involved oral hygiene. Those that aimed to alter sugar intake did not report caries as an outcome variable. |
| Kramer MS Kakuma R (2002) Optimal duration of exclusive breastfeeding. In: The Cochrane Database of Systematic Reviews: Reviews 2002 Issue 1 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003517. | Not a review of interventions to help mothers continue breastfeeding beyond 6 months |
| Kramer MS Kakuma R (2003) Maternal dietary antigen avoidance during pregnancy and/or lactation for preventing or treating atopic disease in the child. In: The Cochrane Database of Systematic Reviews: Reviews 2003 Issue 4 John Wiley & Sons, Ltd Chichester, | Maternal intervention for child health outcome |

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|---|---|
| UK DOI: 10.1002/14651858.CD000133. | |
| Krishna S, Balas EA, Boren SA et al. (2002) Patient acceptance of educational voice messages: a review of controlled clinical studies. Methods of Information in Medicine. 41 (5):360-369. | Not children up to 5 years |
| Kuschel C, Harding JE (1999) Carbohydrate supplementation of human milk to promote growth in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 1999 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000280. | Preterm infants |
| Kuschel C, Harding JE (2000) Protein supplementation of human milk for promoting growth in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2000 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000433. | Preterm infants |
| Kuschel C, Harding JE (2000) Fat supplementation of human milk for promoting growth in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2000 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000341. | Preterm infants |
| Kuschel Ca HJE (2001) Calcium and phosphorus supplementation of human milk for preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2001 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003310. | Preterm infants |
| Kuschel C, Harding JE (2004) Multicomponent fortified human milk for promoting growth in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2004 Issue 1 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000343.pub2. | Preterm infants |
| Lacour M, Zunder T, Restle A et al. (2004) No evidence for an impact of selenium supplementation on environment associated health disorders: a systematic review. International Journal of Hygiene and Environmental Health. 207 (1):1-13. | Not children up to 5 years |
| Lanigan JA, Bishop JA, Kimber AC et al. (2001) Systematic review concerning the age of introduction of complementary foods to the healthy full-term infant. European Journal of Clinical Nutrition. 55 (5):309-320. | Not about timely introduction of supplementary feeds/solids |
| Lucassen P, Assendelft WJ, Jvan Geldrop W (2006) Elimination of cows' milk protein from infant diet for the treatment of infantile colic (Protocol for a Cochrane Review). In: The Cochrane Library, Issue 1. Chichester, UK: John Wiley & Sons, Ltd. | Protocol |
| Mahomed K, Gülmezoglu AM (1997) Maternal iodine supplements in areas of deficiency. In: The Cochrane Database of Systematic Reviews: Reviews 1997 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000135. | Maternal intervention for child health outcome |
| Martins S, Logan S, Gilbert R (2001) Iron therapy for improving psychomotor development and cognitive function in children under the age of three with iron deficiency anaemia. In: The Cochrane Database of Systematic Reviews: Reviews 2001 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001444. | Sick children |
| Osborn Da Sinn J (2006) Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants. In: The Cochrane Database of Systematic Reviews: Reviews 2006 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003664.pub2. | Review has been withdrawn<br><br>NOTE this review was updated and the updated version (Osborn & Sinn 2007) has been included in the review |
| Panpanich RGP (1999) Growth monitoring in children. In: The Cochrane Database of Systematic Reviews: Reviews 1999 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001443. | Not diet |
| Pignone MP, Phillips CJ, Lannon CM et al. (2001) Screening for lipid | Screening |

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|---|---|
| disorders: systematic evidence review.93. | |
| Poustie VJ, Smyth RL, Watling RM (1999) Oral protein calorie supplementation for children with chronic disease. In: The Cochrane Database of Systematic Reviews: Reviews 1999 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001914. | Sick children |
| Ram Fsf, Ducharme FM, Scarlett J (2002) Cow's milk protein avoidance and development of childhood wheeze in children with a family history of atopy. In: The Cochrane Database of Systematic Reviews: Reviews 2002 Issue 1 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD003795. | Study by Chandra in meta-analysis (work discredited) |
| Ramakrishnan U, Aburto N, McCabe G et al. (2004) Multimicronutrient interventions but not vitamin A or iron interventions alone improve child growth: results of 3 meta-analyses. Journal of Nutrition. 134 (10):2592-2602. | Country |
| Sachdev HP, Gera T, Nestel P (2005) Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. Public Health Nutrition. 8 (2):117-132. | Not promotion of supplementation |
| Shepherd J, Harden A, Rees R et al. (2002) Young people and healthy eating: a systematic review of research on barriers and facilitators.165. | Children older than 5 years |
| SIGN (2005) Management of obesity in children and young people. In: Guideline no.69 p.26. | Obesity |
| Simmer K (2001) Longchain polyunsaturated fatty acid supplementation in infants born at term. In: The Cochrane Database of Systematic Reviews: Reviews 2001 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000376. | Formula composition |
| Simmer K, Patole S (2004) Longchain polyunsaturated fatty acid supplementation in preterm infants. In: The Cochrane Database of Systematic Reviews: Reviews 2004 Issue 1 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000375.pub2. | Preterm infants |
| Simons-Morton DG, Mullen PD, Mains DA et al. (1992) Characteristics of controlled studies of patient education and counseling for preventive health behaviors. Patient Education and Counseling. 19 (2):175-204. | No studies on diets of young children |
| Summerbell C, Waters E, Edmunds LD et al. (2005) Interventions for preventing obesity in children. In: The Cochrane Database of Systematic Reviews: Reviews 2005 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001871.pub2. | Obesity |
| Swadling C, Griffiths P (2003) Is modified cow's milk formula effective in reducing the symptoms of infant colic? British Journal of Community Nursing. 8 (1):24-27. | Outcome is not specifically food allergy/intolerance |
| Tang JL, Armitage JM, Lancaster T et al. (1998) Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects. British Medical Journal.1213-1220. | Outcome not among those listed for these 2 reviews |
| Tedstone A, Aviles M, Shetty P et al. (1998) Effectiveness of interventions to promote healthy eating in preschool children aged 1 to 5 years: a review. 65. | Children older than 24 months for outcomes of this Rapid Review |
| Thomas H, Ciliska D, Micucci S et al. (2004) Effectiveness of physical activity enhancement and obesity prevention programs in children and youth.252. | Obesity |
| University of York, N. H. S. Centre for Reviews Dissemination (1997) The prevention and treatment of obesity. Effective Health Care. 3 (2):1-12. | Obesity |
| University of York, N. H. S. Centre for Reviews Dissemination (2002) The prevention and treatment of childhood obesity. Effective Health Care. 7 (6):1-8. | Obesity |

## Excluded RCTs

| Paper – Randomised Controlled Trial | Reason for Exclusion |
|---|---|
| Alarcon PA, Lin LH, Noche M, et al. (2003) Effect of oral supplementation on catch-up growth in picky eaters. Clinical Pediatrics. 42 (3):209-17. | Children older than 24 months |
| Aoki T, Kojima M, Adachi Jet al. (1992) Effect of short-term egg exclusion diet on infantile atopic dermatitis and its relation to egg allergy: a single-blind test. Acta Dermato Venereologica. Supplementum. 176:99-102. | Sick children |
| Arshad H (1993) Effect of food and house dust mite allergen avoidance on development of atopy in infancy. Immunology & Allergy Practice. 15 (7):214. | Not an RCT |
| Becker A, Watson W, Ferguson A et al. (2004) The Canadian asthma primary prevention study: outcomes at 2 years of age. Journal of Allergy & Clinical Immunology. 113 (4):650-6. | Outcomes not reported separately for dietary intervention in the multifaceted intervention |
| Bonuck KA, Trombley M, Freeman K et al. (2005) Randomised, controlled trial of a prenatal and postnatal lactation consultant intervention on duration and intensity of breastfeeding up to 12 months. Pediatrics 116 (6): 1413-26. | Study did not focus on women who planned to return to paid employment. |
| Boulvain M, Perneger TV, Othenin-Girard V et al. (2004) Home-based versus hospital-based postnatal care: a randomised trial. BJOG: An International Journal of Obstetrics and Gynaecology. 111 (8):807-13. | No breastfeeding outcomes beyond 6 months |
| Childs F, Aukett A, Darbyshire P, Ilett S and Livera LN (1997). Dietary education and iron deficiency anaemia in the inner city. Arch Dis Child 76;144-7 | Not included because IDA was not a review question for 6-24m RR (Included in Tedstone 1998 SR) |
| Christofides, A., Schauer, C., Sharieff, W. and Zlotkin, S. H. (2005) Acceptability of micronutrient sprinkles: A new food-based approach for delivering iron to First Nations and Inuit children in Northern Canada. Chronic Dis Can, 26(4), 114-20. | Not supplements |
| Cottrell L, Spangler-Murphy E, Minor V et al. (2005) A kindergarten cardiovascular risk surveillance study: CARDIAC-Kinder. American Journal of Health Behavior. 29 (6):595-606. | Children older than 24 months |
| Cox DR, Skinner JD, Carruth BR et al. (1997) A Food Variety Index for Toddlers (VIT): development and application. Journal of the American Dietetic Association. 97 (12):1382-6; quiz 1387-8. | Not an RCT |
| Deaves DM (1993) An assessment of the value of health education in the prevention of childhood asthma. Journal of Advanced Nursing. 18 (3):354-63. | Children older than 24 months |
| Demas A (1998) Low-fat school lunch programs: achieving acceptance. American Journal of Cardiology. 82 (10B):80T-82T. | Not an RCT |
| Demmers, T. A., Jones, P. J. H., Wang, Y., Krug, S., Creutzinger, V. and Heubi, J. E. (2005) Effects of Early Cholesterol Intake on Cholesterol Biosynthesis and Plasma Lipids Among Infants Until 18 Months of Age. Pediatrics, 115(6), 1594-1601. | Does not address a review question |
| Devenney, I., Norrman, G., Oldaeus, G., Strömberg, L. and Fälth-Magnusson, K. (2006) A new model for low-dose food challenge in children with allergy to milk or egg. Acta Paediatrica, 95(9), 1133-1139. | Sick children |
| Dollahite J, Hosig KW, White K A et al. (1998) Impact of a school-based community intervention program on nutrition knowledge and food choices in elementary school children in the rural Arkansas delta. Journal of Nutrition Education. 30 (5):289-301. | Children older than 24 months |
| Emond A, Pollock J, Deave T, Bonnell S, Peters TJ and Harvey, I (2002). An evaluation of the First Parent Health Visitor Scheme. Arch Dis Child 86; 150-7 | Not an RCT. Not added to UK corroborative studies because no |

| | details of content of the intervention were reported in the paper |
|---|---|
| Estrada-Reyes, E., García-Hernández, G., Martínez-Gimeno, A. and Nava-Ocampo, A. A. (2006) Effect of Extensively Hydrolyzed Milk Formula on Growth and Resistance to Bronchitis and Atopic Dermatitis in Infants and Toddlers. Journal of Investigational Allergology and Clinical Immunology, 16(3), 183-187. | Not an RCT |
| Exl, B. M., U. Deland, et al. (2000). Improved general health status in an unselected infant population following an allergen reduced dietary intervention programme. The ZUFF-study-programme. Part I: Study design and 6-month nutritional behaviour. European Journal of Nutrition 39(3): 89-102. | No relevant outcomes |
| Farrow, C. and J. Blissett (2006). Breast-feeding, maternal feeding practices and mealtime negativity at one year. Appetite 46(1): 49-56. | No intervention |
| Gerrish CJ MJA (2001) Flavor variety enhances food acceptance in formula-fed infants. The American Journal of Clinical Nutrition. 73 (6):1080-1085. | Not an RCT |
| Gibson L (1995) Patient education: effects of two teaching methods upon parental retention of infant feeding practices. Pediatric Nursing. 21 (1):78-80. | No child outcomes |
| Gonzalez-Richmond Ja Naranjo-Banda A (2004) Effect of an integrated nutrition -primary health care package on nutritional status of children. Nutrition Research. 6:1275-1280. | Country (Mexico) |
| Guthrie C, Rapoport L, Wardle J (2000) Young children's food preferences: a comparison of three modalities of food stimuli. Appetite. 35 (1):73-77. | No RR outcomes |
| Horodynski, M. A. and Stommel, M. (2005) Nutrition education aimed at toddlers: An intervention study. Pediatric Nursing 31(5), 364. | Not an RCT |
| Isolauri E, Arvola T, Sutas Y et al. (2000) Probiotics in the management of atopic eczema. Clinical & Experimental Allergy. 30 (11):1604-10. | Sick children |
| Johnson Z, Howell F, Molloy B (1993) Community mothers' programme: randomised controlled trial of non-professional intervention in parenting. BMJ. 306 (6890):1449-52. | Already reported in this Rapid Review as part of Elkan's systematic review |
| Johnston, B. D., Huebner, C. E., Anderson, M. L., Tyll, L. T. and Thompson, R. S. (2006) Healthy Steps in an Integrated Delivery System: Child and Parent Outcomes at 30 Months. Archives of Pediatrics and Adolescent Medicine, 160(8), 793. | No RR outcomes |
| Juvonen P, Mansson M, Andersson C et al. (1996) Allergy development and macromolecular absorption in infants with different feeding regimens during the first three days of life. A three-year prospective follow-up. Acta Paediatrica. 85 (9):1047-52. | Intervention during first 3 days of life only Included in SR by Osborn and Sinn 2006 in this review |
| Kaitosaari, T., T. Ronnemaa, et al. (2006). Low-saturated fat dietary counseling starting in infancy improves insulin sensitivity in 9-year-old healthy children: the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study. Diabetes Care 29(4): 781-5. | i) Long-term outcomes and not relevant to this review |
| Kimbro, R. T. (2006). On-the-job moms: Work and breastfeeding initiation and duration for a sample of low-income women. Maternal & Child Health Journal 10(1): 19-26. | Cohort study |
| Kirjavainen PV, Salminen SJ, Isolauri E (2003) Probiotic bacteria in the management of atopic disease: underscoring the importance of viability. Journal of Pediatric Gastroenterology & Nutrition. 36 (2):223-7. | Sick children |
| Krebs, N. F., Westcott, J. E., Butler, N., Robinson, C., Bell, M. and | No RR outcomes |

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|---|---|
| Hambidge, K. M. (2006) Meat as a first complementary food for breastfed infants: feasibility and impact on zinc intake and status. J Pediatr Gastroenterol Nutr, 42(2), 207-214. | |
| Lever R, MacDonald C, Waugh P et al. (1998) Randomised controlled trial of advice on an egg exclusion diet in young children with atopic eczema and sensitivity to eggs. Pediatric Allergy & Immunology 9(1):13-9. | Sick children |
| Mabin DC, Sykes A E, David TJ (1995) Controlled trial of a few foods diet in severe atopic dermatitis. Archives of Disease in Childhood. 73 (3):202-7. | Sick children |
| Mallet, E. and A. Henocq (1992). Long-term prevention of allergic diseases by using protein hydrolysate formula in at-risk infants. Journal of Pediatrics 121(5 Pt 2): S95-100. | Included in SR by Osborn and Sinn 2006 in this review |
| Marini, A., Agosti, M., Motta, G. and Mosca, F. (1996) Effects of a dietary and environmental prevention programme on the incidence of allergic symptoms in high atopic risk infants: three years' follow-up. Acta Paediatr Suppl, 414, 1-21. | Included in SR by Osborn and Sinn 2006 in this review |
| Mehta KC, Specker BL, Bartholmey S et al. (1998) Trial on timing of introduction to solids and food type on infant growth. Pediatrics. 102 (3 Pt 1):569-73. | Not about timely introduction of appropriate weaning foods |
| Mihrshahi S, Peat JK, Webb K et al. (2004) Effect of omega-3 fatty acid concentrations in plasma on symptoms of asthma at 18 months of age. Pediatric Allergy & Immunology. 15 (6):517-22. | RCT included in review by Tricon et al 2006 included in 2-5 year NICE RR |
| Mongeon, M. and Allard, R. (1995) A controlled trial of rebular telephonic support given by volunteers on the progress and outcome of breast-feeding. Original: Essai controle d'un soutien telephonique regulier donne par une benevole sur le deroulement et l'issue de l'allaitment. Canadian Journal of Public Health 86 (2): 124-127. | Intervention does not specifically focus on breastfeeding beyond 6 months |
| Moss, M. H. (2005). Endotoxin exposure and eczema in the first year of life. Pediatrics 116(2): 541. | Irrelevant intervention – exposure to dust |
| Muirhead PE, Butcher G, Rankin J et al. (2006) The effect of a programme of organised and supervised peer support on the initiation and duration of breastfeeding: A randomised trial. British Journal of General Practice. 56 (524):191-197. | Last breastfeeding outcome 16 weeks |
| Niinikoski, H., J. Viikari, et al. (1996). Prospective randomized trial of low-saturated-fat, low-cholesterol diet during the first 3 years of life. The STRIP baby project. Circulation 94(6): 1386-93. | Included in SR in this RR - Tedstone et al 1998 |
| Nossar V, Hudson D (2001) Improving health outcomes for children by home visiting. Medicine Today. 2 (8):135-136. | Not an RCT |
| Oscarson R, Branum J (1999) A soybean education curriculum for preschoolers: introducing new foods to children. Journal of Family and Consumer Sciences: From Research to Practice. 91 (1):59-64. | Children older than 24 months |
| Peat JK, Mihrshahi S, Kemp AS et al. (2004) Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. Journal of Allergy & Clinical Immunology. 114 (4):807-13. | Children older than 24 months |
| Raynor P, Rudolf MC, Cooper K et al. (1999) A randomised controlled trial of specialist health visitor intervention for failure to thrive. Archives of Disease in Childhood. 80 (6):500-6. | Sick children |
| Rosenfeldt V, Benfeldt E, Nielsen SD et al. (2003) Effect of probiotic Lactobacillus strains in children with atopic dermatitis. Journal of Allergy & Clinical Immunology. 111 (2):389-95. | Sick children |
| Rosenfeldt V, Benfeldt E, Valerius NH et al. (2004) Effect of probiotics on gastrointestinal symptoms and small intestinal permeability in children with atopic dermatitis. Journal of Pediatrics. 145 (5):612-6. | Sick children |
| Roy, S. K., Fuchs, G. J., Mahmud, Z., Ara, G., Islam, S., Shafique, S., Akter, S. S. and Chakraborty, B. (2005) Intensive Nutrition Education | Country |

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|---|---|
| with or without Supplementary Feeding Improves the Nutritional Status of Moderately-malnourished Children in Bangladesh. Journal of Health, Population and Nutrition, 23(4), 320-330. | |
| Sappo L, Korpela R, Lonnerdal B et al. (2005) A Follow-up Study of Nutrient Intake, Nutritional Status, and Growth in Infants with Cow Milk Allergy Fed Either a Soy Formula or an Extensively Hydrolysed Whey Formula. Journal of Pediatric Gastroenterology and Nutrition, 42(5), 594. | Sick children |
| Shah M, Griffin IJ, Lifschitz CH et al. (2003) Effect of orange and apple juices on iron absorption in children. Archives of Pediatrics & Adolescent Medicine. 157 (12):1232-6. | Children older than 24 months |
| Sharma, M. and Kanani, S. (2006) Grandmothers'Influence on Child Care. Indian Journal of Pediatrics, 73, 295. | Not an RCT |
| Spigelblatt L, Laine-Ammara G, Arsenault L et al. (1991) [Influence of follow-up education of mothers about too early introduction of solid food to infants]. Revista de pediatrie Full details of publication on the link: Revista de pediatrie, obstetrica si ginecologie. Pediatria. PUBMED 1663244. Cochrane ID: CN-00081014. 46 (5):475-9. | Paper is in French only |
| Sritharan N, Morgan J (2002) Infant meal planners: A risk or remedy to the health of infants? Nutrition Bulletin. 27 (4):241-242. | Not an RCT |
| Staab D, Von Rueden U, Kehrt R et al. (2002) Evaluation of a parental training program for the management of childhood atopic dermatitis. Pediatric Allergy & Immunology. 13 (2):84-90. | Sick children |
| Tsai YT, Chou CC, Hsieh KH (1991) The effect of hypoallergenic formula on the occurrence of allergic diseases in high risk infants. In: 1991. | No outcomes later than 6 months Included in SR by Osborn and Sinn 2006 in this review |
| Vandenplas Y, Hauser B, Van den Borre C et al. (1995) The long-term effect of a partial whey hydrolysate formula on the prophylaxis of atopic disease. European Journal of Pediatrics. 154 (6):488-94. | Children older than 24 months Included in SR by Osborn and Sinn 2006 in this review |
| Viljanen, M., Savilahti, E., Haahtela, T., Juntunen-Backman, K., Korpela, R., Poussa, T., Tuure, T. and Kuitunen, M. (2005) Probiotics in the treatment of atopic eczema/dermatitis syndrome in infants: a double-blind placebo-controlled trial. Allergy, 60(4), 494-500. | Sick children |
| Vitolo, M. R., Bortolini, G. A., Feldens, C. A. and Drachler, M. L. (2005) Impacts of the 10 Steps to Healthy Feeding in Infants: a randomized field trial. Cadernos de Sade Publica, 21, 1448-1457. | Not published in English |
| Wardle J, Cooke LJ, Gibson EL et al. (2003) Increasing children's acceptance of vegetables; a randomized trial of parent-led exposure. Appetite. 40 (2):155-62. | Children older than 24 months |
| Warschburger P, von Schwerin AD, Buchholz HT et al. (2003) An educational program for parents of asthmatic preschool children: short- and medium-term effects. Patient Education & Counseling. 51 (1):83-91. | Sick children |
| Weston S, Halbert A, Richmond P et al. (2005) Effects of probiotics on atopic dermatitis: a randomised controlled trial. Archives of Disease in Childhood. 90 (9):892-7. | Sick children |
| Weston, S., Halbert, A., Richmond, P. and Prescott, S. L. (2005) Effects of probiotics on atopic dermatitis: a randomised controlled trial. Royal College of Paediatrics. | Sick children |
| Witters-Green R (2003) Increasing Breastfeeding Rates in Working Mothers. Families, Systems, & Health. 21 (4):415-434. | Not an RCT |
| Zutavern, A., von Mutius, E., Harris, J., Mills, P., Moffatt, S., White, C. and Cullinan, P. (2004) The introduction of solids in relation to asthma and eczema. Royal College of Paediatrics. | Not an RCT |

**Excluded evidence consultation stakeholder papers**

As part of the NICE evidence synopsis consultation process, some papers were identified as being relevant by stakeholders. References, brief descriptions and reasons for exclusion of these additional papers appear in the table below.

| Reference | Description | Reason for exclusion |
|---|---|---|
| Lucas et al (1990) Early diet of preterm infants and development of allergic or atopic disease: randomised prospective study. BMJ 300 pp 837-840 | Reports two randomised prospective trials involving 777 preterm infants with birth weight less than 1850g. Compared donor milk with preterm formula, and term with preterm formula, as a supplement to mother's expressed breast milk. At 18 months after term no difference was found in the incidence of allergic reactions between dietary groups in either trial. | Identified in original search<br>Excluded<br>Did not meet criteria (i.e. did not include preterm infants) |
| Kramer MS (1988) Does breast feeding help protect against atopic disease? Biology, methodology and a golden jubilee of controversy. The Journal of Pediatrics Vol. 112, No.2, Feb, pp 181-90 | Reports the results of a Medline search for articles on this topic, that were graded according to 12 standards by the author, who found that serious flaws reduced the value of all studies in greater or lesser degree. | Excluded<br>Date (was limited to studies published in 1990 or later)<br><br>Possible background |
| Zeiger RS, Heller S (1995) The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomised study of combined maternal and infant food allergen avoidance. J Allergy Clin Immunol 95(6) (June):1179-90 | *Participants*: High-risk cohort, 165 children, previously reported from birth to four years<br>*Intervention*: mothers avoided cow's milk, egg, and peanut during the last trimester of pregnancy and lactation; infants until age 1 year (casein hydrolysate supplementation before age 1), egg until age 2 years, and peanut and fish until age 3 years.<br>*Control*: standard feeding practices (not described).<br>*Outcomes & Significance:* a significant reduction in food allergy and milk sensitisation before age 2 years. Among children with food allergy by 4 years higher rates of asthma and allergic rhinitis were found (p<0.01). Other measures at age 7 did not differ between the groups. | Excluded<br>Date<br>This paper was reporting 7 year outcomes of a study originally published before 1990.<br><br>The original publication was:<br>Zeiger et al (1989) Effect of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: a randomised study. J Allergy Clin Immunol vol 84 pp 72-89)<br><br>Possible background |

## APPENDIX C – Search strategy

Searches for NICE Rapid Review "The effectiveness of public health interventions to improve the nutrition of young children aged 6 months to 5 years".

### Search for systematic reviews (12/04/06)

| Resource | Issue/ search date | Records | After dedupe | Custom 4 code |
|---|---|---|---|---|
| CDSR | 2006/2 25/04/06 | 118 | 75 | cdsr sr child nutrition |
| DARE | 25/04/06 | 171 | 79 | dare sr child nutrition |
| NRR | 2006/1 25/04/06 | 75 28 118 36 126 8 745 105 | 505 | NRR_MultiCentreComplete SR child nutrition NRR_MultiCentreOngoing SR child nutrition NRR_ParticipCentreComplete SR child nutrition NRR_ParticipCentreOngoing SR child nutrition NRR_RegandNatComplete SR child nutrition NRR_RegandNatOngoing SR child nutrition NRR_SingleCentreComplete SR child nutrition NRR_SingleCentreOngoing SR child nutrition |
| HTA | 25/04/06 | 16 | 14 | hta sr child nutrition |
| SIGN | 12/04/06 | 2 | 2 | sign sr child nutrition |
| NGC | 24/04/06 | 10 | 10 | ngc sr child nutrition |
| NCCHTA | 12/04/06 | 0 | | NA |
| NICE | 14/04/06 | 0 | | NA |
| HSTAT | 24/02/06 | 3 relevant records | 3 | hstat sr child nutrition |
| ReFeR | 20/2/06 | 4 relevant records | 4 | refer sr child nutrition |
| Clinical Evidence | 25/02/06 | 0 | | NA |
| HEBW | 25/02/06 | 1 chapter relevant | 1 | hebw sr child nutrition |
| TRIP | 25/02/06 | 0 | | NA |

The following search terms were used to identify relevant systematic reviews (from 1995 onwards):

**Cochrane Database of Systematic Reviews (CDSR)**
http://www.cochrane.org/reviews/clibintro.htm

The online Cochrane Library was searched. The strategy used a combination of MeSH subject headings and text searches. The search is focused on 'population', 'interventions' and 'outcomes'. The search located 118 systematic reviews.

| ID | Search | Records |
|----|--------|---------|
| #1 | MeSH descriptor Infant, this term only in MeSH products | 6 |
| #2 | MeSH descriptor Child explode all trees in MeSH products | 9 |
| #3 | infant* or preschool* or pre*school or "pre school" or nurser* or playschool* or kindergarten* or creche* or pre*school* or "pre school" in Title, Abstract or Keywords in all products | 30395 |
| #4 | (#1 OR #2 OR #3) | 30396 |
| #5 | <nothing>, from 1995 to 2006 in all products | 292971 |
| #6 | (#4 AND #5) | 17724 |
| #7 | ((food* or nutrition* or diet* or nutritive or feed* or eating or health) near/3 (supplement* or habit* or behavior* or behaviour* or attitude* or belief* or polic* or value*)) in Title, Abstract or Keywords in all products | 11135 |
| #8 | solid food or solids or baby food* in Title, Abstract or Keywords in all products | 1738 |
| #9 | wean* or weaning in Title, Abstract or Keywords in all products | 848 |
| #10 | MeSH descriptor Weaning, this term only in MeSH products | 52 |
| #11 | family food in Title, Abstract or Keywords in all products | 198 |
| #12 | MeSH descriptor Fruit explode all trees in MeSH products | 425 |
| #13 | MeSH descriptor Vegetables, this term only in MeSH products | 322 |
| #14 | fruit* or vegetable* in Title, Abstract or Keywords in all products | 1378 |
| #15 | MeSH descriptor Sodium, Dietary explode all trees in MeSH products | 335 |
| #16 | sodium in Title, Abstract or Keywords in all products | 14226 |
| #17 | vitamin* or iron or mineral* in Title, Abstract or Keywords in all products | 11357 |
| #18 | MeSH descriptor Vitamins explode all trees in MeSH products | 2 |
| #19 | MeSH descriptor Minerals explode all trees in MeSH products | 1617 |
| #20 | MeSH descriptor Food Habits, this term only in MeSH products | 411 |

| | | |
|---|---|---|
| #21 | MeSH descriptor Food explode all trees in MeSH products | 9669 |
| #22 | MeSH descriptor Nutrition, this term only in MeSH products | 527 |
| #23 | MeSH descriptor Nutrition Policy, this term only in MeSH products | 57 |
| #24 | MeSH descriptor Diet, this term only in MeSH products | 2108 |
| #25 | MeSH descriptor Feeding Behavior, this term only in MeSH products | 351 |
| #26 | MeSH descriptor Health Behavior, this term only in MeSH products | 738 |
| #27 | (nutrition* or nutrient* or micronutrient* or diet* or energy) near/3 (intake or advice or counsel* or education or supplement* or requirement* or value) in Title, Abstract or Keywords in all products | 8937 |
| #28 | MeSH descriptor Energy Intake, this term only in MeSH products | 1786 |
| #29 | MeSH descriptor Nutritional Requirements, this term only in MeSH products | 296 |
| #30 | MeSH descriptor Nutritive Value, this term only in MeSH products | 99 |
| #31 | nutrition* near/3 knowledge in Title, Abstract or Keywords in all products | 98 |
| #32 | MeSH descriptor Breast Feeding, this term only in MeSH products | 708 |
| #33 | breastfeeding or breastfed in Title, Abstract or Keywords in all products | 481 |
| #34 | ((salt or sugar) near/3 (intake or consumption)) or soft drink* or soda or candy or chocolate or sweets or confection* in Title, Abstract or Keywords in all products | 914 |
| #35 | MeSH descriptor Carbonated Beverages, this term only in MeSH products | 38 |
| #36 | MeSH descriptor Cacao, this term only in MeSH products | 65 |
| #37 | MeSH descriptor Candy, this term only in MeSH products | 31 |
| #38 | (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37) | 47367 |
| #39 | (#6 AND #38) | 3294 |
| #40 | MeSH descriptor Infant Food explode all trees in MeSH products | 818 |
| #41 | MeSH descriptor Infant Nutrition, this term only in MeSH products | 421 |
| #42 | MeSH descriptor Child Nutrition, this term only in MeSH products | 169 |
| #43 | (infant or child) near/3 (food* or nutrition* or feed*) in Title, | 2241 |

**Abstract or Keywords in all products**

| | | |
|---|---|---|
| #44 | (#40 OR #41 OR #42 OR #43) | 2271 |
| #45 | \<nothing\>, from 1995 to 2006 in all products | 292971 |
| #46 | (#44 AND #45) | 1335 |
| #47 | (#39 OR #46) | 3647 |
| #48 | MeSH descriptor Food Hypersensitivity explode all trees in MeSH products | 386 |
| #49 | food near/3 (allerg* or sensitiv*) in Title, Abstract or Keywords in all products | 256 |
| #50 | MeSH descriptor Dental Caries, this term only in MeSH products | 843 |
| #51 | MeSH descriptor Tooth Loss, this term only in MeSH products | 21 |
| #52 | MeSH descriptor Tooth Erosion, this term only in MeSH products | 57 |
| #53 | dental caries or ((dental or tooth) near/3 (loss or decay or erosion)) in Title, Abstract or Keywords in all products | 1622 |
| #54 | MeSH descriptor Nutritional Status, this term only in MeSH products | 788 |
| #55 | MeSH descriptor Growth, this term only in MeSH products | 547 |
| #56 | MeSH descriptor Body Weight, this term only in MeSH products | 4004 |
| #57 | MeSH descriptor Malnutrition, this term only in MeSH products | 42 |
| #58 | nutritional status or body weight or bodyweight or malnutrition in Title, Abstract or Keywords in all products | 13734 |
| #59 | MeSH descriptor Thinness, this term only in MeSH products | 43 |
| #60 | MeSH descriptor Obesity, this term only in MeSH products | 2948 |
| #61 | overweight or obes* or thinness or (body near/3 (height or size)) in Title, Abstract or Keywords in all products | 6339 |
| #62 | MeSH descriptor Body Height, this term only in MeSH products | 830 |
| #63 | MeSH descriptor Body Size, this term only in MeSH products | 31 |
| #64 | MeSH descriptor Child Development, this term only in MeSH products | 623 |
| #65 | child* near/3 (development or growth) in Title, Abstract or Keywords in all products | 1487 |
| #66 | breastfeeding near/4 (length or duration) in Title, Abstract or Keywords in all products | 92 |
| #67 | MeSH descriptor Rickets, this term only in MeSH products | 24 |

| | | |
|---|---|---|
| #68 | rickets in Title, Abstract or Keywords in all products | 61 |
| #69 | (nutrition* or nutrient* or micronutrient* or diet* or energy) near/3 (intake or advice or counsel* or education or supplement* or requirement* or value) in Title, Abstract or Keywords in all products in All Fields in all products | 360066 |
| #70 | MeSH descriptor Energy Intake, this term only in MeSH products in All Fields in all products | 976 |
| #71 | MeSH descriptor Nutritive Value, this term only in MeSH products in All Fields in all products | 976 |
| #72 | MeSH descriptor Nutritional Requirements, this term only in MeSH products in All Fields in all products | 976 |
| #73 | MeSH descriptor Nutritional Requirements, this term only in MeSH products in All Fields in all products | 976 |
| #74 | MeSH descriptor Anemia, Iron-Deficiency, this term only in MeSH products | 286 |
| #75 | anemi* or aenemi* or iron deficien* in Title, Abstract or Keywords in all products | 3430 |
| #76 | MeSH descriptor Gastrointestinal Diseases explode all trees in MeSH products | 15511 |
| #77 | MeSH descriptor Parasitic Diseases explode all trees in MeSH products | 3505 |
| #78 | (parasitic or gastrointestinal or respiratory) near/3 (disease* or infection* or parasite*) in Title, Abstract or Keywords in all products | 5059 |
| #79 | MeSH descriptor Respiratory Tract Diseases explode all trees in MeSH products | 26648 |
| #80 | MeSH descriptor Asthma, this term only in MeSH products | 6965 |
| #81 | MeSH descriptor Eczema, this term only in MeSH products | 266 |
| #82 | asthma or eczema or wheeze in Title, Abstract or Keywords in all products | 15586 |
| #83 | MeSH descriptor Mortality, this term only in MeSH products | 262 |
| #84 | MeSH descriptor Infant Mortality, this term only in MeSH products | 293 |
| #85 | MeSH descriptor Morbidity, this term only in MeSH products | 535 |
| #86 | mortality or morbidity in Title, Abstract or Keywords in all products | 26064 |
| #87 | MeSH descriptor Health Knowledge, Attitudes, Practice, this term only in MeSH products | 1360 |

| | | |
|---|---|---|
| #88 | health near/3 (knowledge or attitude* or practice*) in Title, Abstract or Keywords in all products | 4218 |
| #89 | MeSH descriptor Maternal Behavior, this term only in MeSH products | 93 |
| #90 | MeSH descriptor Paternal Behavior, this term only in MeSH products | 4 |
| #91 | (maternal or paternal or mother* or father* or parent* or carer*) near/3 (behavior* or behaviour* or knowledge or practice*) in Title, Abstract or Keywords in all products | 767 |
| #92 | (#48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91) | 379396 |
| #93 | (#47 AND #92) | 3400 |

(Hits shown are for all records in Cochrane Library- not just Cochrane reviews. Of the 3400 final hits, 118 were Cochrane reviews.)

**Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database**

This search used the CRD DARE admin database (Cairs B), which contains DARE records and CDSR abstracts, and the CRD HTA admin database. The search is focused on 'population' and 'interventions'. The search located 171 reviews in DARE and 16 in HTA.

1. S infant /kwo
2. S child /kwo
3. S (infant$ or child$ or preschool$ or nurser$ or playschool$ or crèche$ or kindergarten$)
4. S s1 or s2 or s3
5. S (wean$ or fruit$ or vegetable$ or nutrient$ or micronutrient$ or salt or sugar or soda or candy or chocolate or sweets or confection$ or soft(w)drinks)
6. S weaning /kwo
7. S fruit /kwo
8. S vegetables /kwo
9. S sodium dietary /kwo
10. S vitamins /kwo
11. S minerals /kwo
12. S food /kwo
13. S food habits /kwo
14. S nutrition /kwo
15. S nutrition policy/ kwo
16. S diet/ kwo
17. S feeding behavior /kwo
18. S health behavior /kwo
19. S energy intake /kwo
20. S nutritional requirements /kwo

21. S nutritive value /kwo
22. S breast feeding /kwo
23. S carbonated beverages /kwo
24. S cacao /kwo
25. S candy /kwo
26. s s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14 or s15 or s16 or s17 or s18 or s19 or s20 or s21 or s22 or s23 or s24 or s25
27. s s4 and s26
28. S infant food /kwo
29. S infant nutrition /kwo
30. S child nutrition /kwo
31. s infant$ (3w) food$
32. s infant$ (3w) diet$
33. s infant$ (3w) nutrition$
34. s infant$ (3w) feed$
35. s child$ (3w) food$
36. s child$ (3w) diet$
37. s child$ (3w) nutrition$
38. s child$ (3w) feed$
39. s s28 or s29 or s30 or s31 or s32 or s33 or s34 or s35 or s36 or s37 or s38
40. s s27 or s39


**National Research Register (NRR) (including CRD ongoing reviews)**
http://www.nrr.nhs.uk/

| | | |
|---|---|---|
| #1. | INFANT single term (MeSH) | 1464 |
| #2. | CHILD explode all trees (MeSH) | 7457 |
| #3. | (#1 or #2) | 8173 |
| #4. | (food* or nutrition* or diet* or nutritive or feed* or eating:ti) | 6314 |
| #5. | ((solid next food) or solids or (baby next food*) or wean* or (family next food) or fruit* or vegetable* or nutrient* or micronutrient* or salt or sugar or (soft next drink*) or soda or candy or chocolate or sweets or confection*) | 1185 |
| #6. | WEANING single term (MeSH) | 18 |
| #7. | FRUIT explode all trees (MeSH) | 35 |
| #8. | VEGETABLES single term (MeSH) | 22 |
| #9. | SODIUM DIETARY explode all trees (MeSH) | 18 |
| #10. | VITAMINS explode all trees (MeSH) | 683 |
| #11. | MINERALS explode all trees (MeSH) | 108 |
| #12. | FOOD explode all trees (MeSH) | 680 |
| #13. | FOOD HABITS single term (MeSH) | 77 |
| #14. | NUTRITION single term (MeSH) | 79 |
| #15. | NUTRITION POLICY single term (MeSH) | 3 |
| #16. | DIET single term (MeSH) | 488 |
| #17. | FEEDING BEHAVIOR single term (MeSH) | 51 |
| #18. | HEALTH BEHAVIOR single term (MeSH) | 142 |

| #19. ENERGY INTAKE single term (MeSH) | 46 |
|---|---|
| #20. NUTRITIONAL REQUIREMENTS single term (MeSH) | 9 |
| #21. NUTRITIVE VALUE single term (MeSH) | 1 |
| #22. BREAST FEEDING single term (MeSH) | 160 |
| #23. CARBONATED BEVERAGES single term (MeSH) | 3 |
| #24. CACAO single term (MeSH) | 1 |
| #25. CANDY single term (MeSH) | 2 |
| #26. (#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25) | 7861 |
| #27. (#3 and #26) | 789 |
| #28. INFANT FOOD explode all trees (MeSH) | 30 |
| #29. INFANT NUTRITION single term (MeSH) | 74 |
| #30. CHILD NUTRITION single term (MeSH) | 40 |
| #31. (infant next food) | 31 |
| #32. (infant next diet*) | 7 |
| #33. (infant next nutrition*) | 80 |
| #34. (infant next feed*) | 82 |
| #35. (child next feed*) | 4 |
| #36. (child next food*) | 1 |
| #37. (child next diet*) | 3 |
| #38. (child next nutrition*) | 52 |
| #39. (#28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38) | 216 |
| #40. (#27 or #39) | 894 |
| #41. infant*:ti | 1566 |
| #42. child*:ti | 8184 |
| #43. preschool*:ti | 29 |
| #44. nurser*:ti | 18 |
| #45. playschool:ti | 0 |
| #46. kindergarten:ti | 0 |
| #47. creche:ti | 0 |
| #48. (#41 or #42 or #43 or #44 or #45 or #46 or #47) | 9654 |
| #49. (#48 and #26) | 973 |
| #50. (#27 or #39 or #49) | 1316 |

**Scottish Intercollegiate Guidelines Network (SIGN)**
http://www.sign.ac.uk/guidelines/published/numlist.html
Examined full list of titles- 2 relevant under 'child health'.

**National Guideline Clearinghouse (NGC)**
http://www.guideline.gov/

(child* or infant*) and ("diet*" or nutrition or "food*" or "feed*")
775 results screened by hand. 10 relevant results added to Endnote library.

**National Coordinating Centre for Health Technology Assessment (NCCHTA)**
http://www.hta.nhsweb.nhs.uk/projectdata/1_project_listings.asp
Examined all records in category 'children and younger people' – none relevant.

**National Institute for Health and Clinical Excellence (NICE)**
http://www.nice.org.uk/
Looked at guidelines under the topics 'Gynecology, pregnancy and birth' and ' Mouth and dental'.
Searched using search terms: food, feed, nutrition, child and infant.
No relevant results.

**Health Services Technology Assessment Text (HSTAT)**
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
infant food AND book [hstat]
infant feed AND book [hstat]
infant nutrition book [hstat]
child food AND book [hstat]
child feed AND book [hstat]
child nutrition AND book [hstat]
All results checked- 3 relevant added to Endnote library.

**Clinical Evidence**
Searched hard copy - no relevant chapters found.

**Health Evidence Bulletins Wales (HEBW)**
http://hebw.cf.ac.uk/
Searched all records on 'child health' and 'nutrition' – one bulletin relevant 'Maternal and Early Child Health' (Jan 1998). Link added to Endnote library.

**Research Findings Register (RefeR)**
http://www.info.doh.gov.uk/doh/refr_web.nsf/Home?OpenForm
diet* or nutrition* or food* or feed*
All results checked- 4 relevant added to Endnote library.

**Turning Research Into Practice (TRIP)**
http://www.tripdatabase.com/index.html
(nutrition or diet* or food$ or feed*) and child*
(nutrition or diet* or food$ or feed*) and infant*
5 relevant SRs identified all previously identified in searches of CDSR, DARE and HEBW.

## Search for RCTs (April 2006)

A combined strategy was developed and approved from the draft strategies for infants (6-24 months), and preschool children (2 years to 5 years). The strategy was;

**(a) run in Medline for 1990 onwards, with the addition of an RCT filter, excluding developing countries (using MeSH terms), and restricted to English language studies.**

Database: Ovid MEDLINE(R) 1966 to April Week 3 2006
1    infant/ or (infant or infants).ti,ab. (544028)
2    child, preschool/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (567032)
3    or/1-2 (813397)
4    limit 3 to (english language and yr="1990 - 2006") (337550)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (68072)
6    (solid food or solids or baby food$).ti,ab. (6305)
7    weaning/ or (wean$ or weaning).ti,ab. (24735)
8    family food.ti,ab. (64)
9    exp fruit/ or vegetables/ or fruit$.ti,ab. or vegetable$.ti,ab. (53926)
10    sodium, dietary/ or sodium.ti,ab. (186306)
11    sodium chloride, dietary/ (1858)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (259600)
13    minerals.ti,ab. or exp minerals/ (69562)
14    food habits/ or exp food/ or nutrition/ or nutrition policy/ (451147)
15    health behavior/ or diet/ or feeding behavior/ (102527)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutritive value/ (79802)
17    (nutrition$ adj3 knowledge).ti,ab. (717)
18    breastfeeding.ti,ab. or breastfeeding/ (18800)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or candy/ (10205)
20    or/5-19 (1069244)
21    4 and 20 (30858)
22    infant food/ or infant nutrition/ or (infant adj3 (food$ or nutrition)).ti,ab. (15242)
23    child nutrition/ or (child$ adj3 (food$ or nutrition)).ti,ab. (7510)
24    or/22-23 (21592)
25    limit 24 to (english language and yr="1990 - 2006") (8756)
26    21 or 25 (33704)
27    exp food hypersensitivity/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (10200)
28    exp dental caries/ or dental caries.ti,ab. or tooth loss/ or tooth erosion/ or (tooth adj4 (loss or erosion or decay)).ti,ab. (31122)
29    nutritional status/ or nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body weight changes/ or weight.ti,ab. or bodyweight.ti,ab. or malnutrition/ or malnutrition.ti,ab. (944319)
30    overweight/ or overweight.ti,ab. or obes$.ti,ab. or thinness/ or thinness.ti,ab. or body height/ or body size/ or (body adj4 (height or size)).ti,ab. (105314)
31    child development/ or (child$ adj3 (development or growth)).ti,ab. (34873)

32    (breastfeeding adj3 (length or duration)).ti,ab. (719)
33    rickets/ or rickets.ti,ab. (5073)
34    ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutritive value/ (67225)
35    (anemi$ or anaemi$).ti,ab. or anemia, iron deficiency/ or iron deficien$.ti,ab. (69682)
36    exp gastrointestinal diseases/ (494192)
37    exp parasitic diseases/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (247196)
38    exp respiratory tract diseases/ (690651)
39    Asthma/ or (asthma or wheeze).ti,ab. (85689)
40    Eczema/ or eczema.ti,ab. (9424)
41    mortality/ or infant mortality/ or mortality.ti,ab. (247406)
42    Morbidity/ or morbidity.ti,ab. (128904)
43    health knowledge, attitudes, practice/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (39326)
44    maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (13639)
45    paternal behavior/ (884)
46    or/27-45 (2679767)
47    26 and 46 (19561)
48    exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (439496)
49    developing countries/ (45951)
50    or/48-49 (456371)
51    47 not 50 (15364)
52    clinical trial.pt. (428181)
53    (randomized or placebo).ab. or clinical trials/ (300865)
54    randomly.ab. or trial.ti. (151868)
55    or/52-54 (607054)
56    51 and 55 (2574)
57    animals/ not (animals/ and humans/) (2962375)
58    56 not 57 (2511)
59    from 58 keep 1-2511 (2511)

**(b) run for 1990- 2006 in CENTRAL (without the RCT filter).**

| ID | Search | Hits |
|---|---|---|
| #1 | MeSH descriptor **Infant**, this term only in **MeSH products** | 6 |
| #2 | MeSH descriptor **Child** explode all trees in **MeSH products** | 9 |
| #3 | **infant\* or preschool\* or pre\*school or "pre school" or nurser\* or playschool\* or kindergarten\* or creche\* or pre\*school\* or "pre school"** in **Title, Abstract or Keywords** in **all products** | 30395 |
| #4 | (**#1** OR **#2** OR **#3**) | 30396 |
| #5 | **<nothing>**, from 1990 to 2006 in **all products** | 377491 |

| | | |
|---|---|---|
| #6 | (#4 AND #5) | 22878 |
| #7 | ((food* or nutrition* or diet* or nutritive or feed* or eating or health) near/3 (supplement* or habit* or behavior* or behaviour* or attitude* or belief* or polic* or value*)) in Title, Abstract or Keywords in all products | 11135 |
| #8 | solid food or solids or baby food* in Title, Abstract or Keywords in all products | 1738 |
| #9 | wean* or weaning in Title, Abstract or Keywords in all products | 848 |
| #10 | MeSH descriptor Weaning, this term only in MeSH products | 52 |
| #11 | family food in Title, Abstract or Keywords in all products | 198 |
| #12 | MeSH descriptor Fruit explode all trees in MeSH products | 425 |
| #13 | MeSH descriptor Vegetables, this term only in MeSH products | 322 |
| #14 | fruit* or vegetable* in Title, Abstract or Keywords in all products | 1378 |
| #15 | MeSH descriptor Sodium, Dietary explode all trees in MeSH products | 335 |
| #16 | sodium in Title, Abstract or Keywords in all products | 14226 |
| #17 | vitamin* or iron or mineral* in Title, Abstract or Keywords in all products | 11357 |
| #18 | MeSH descriptor Vitamins explode all trees in MeSH products | 2 |
| #19 | MeSH descriptor Minerals explode all trees in MeSH products | 1617 |
| #20 | MeSH descriptor Food Habits, this term only in MeSH products | 411 |
| #21 | MeSH descriptor Food explode all trees in MeSH products | 9669 |
| #22 | MeSH descriptor Nutrition, this term only in MeSH products | 527 |
| #23 | MeSH descriptor Nutrition Policy, this term only in MeSH products | 57 |
| #24 | MeSH descriptor Diet, this term only in MeSH products | 2108 |
| #25 | MeSH descriptor Feeding Behavior, this term only in MeSH products | 351 |

| | | |
|---|---|---|
| #26 | MeSH descriptor **Health Behavior**, this term only in **MeSH products** | 738 |
| #27 | **(nutrition\* or nutrient\* or micronutrient\* or diet\* or energy) near/3 (intake or advice or counsel\* or education or supplement\* or requirement\* or value)** in **Title, Abstract or Keywords** in **all products** | 8937 |
| #28 | MeSH descriptor **Energy Intake**, this term only in **MeSH products** | 1786 |
| #29 | MeSH descriptor **Nutritional Requirements**, this term only in **MeSH products** | 296 |
| #30 | MeSH descriptor **Nutritive Value**, this term only in **MeSH products** | 99 |
| #31 | **nutrition\* near/3 knowledge** in **Title, Abstract or Keywords** in **all products** | 98 |
| #32 | MeSH descriptor **Breast Feeding**, this term only in **MeSH products** | 708 |
| #33 | **breastfeeding or breastfed** in **Title, Abstract or Keywords** in **all products** | 481 |
| #34 | **((salt or sugar) near/3 (intake or consumption)) or soft drink\* or soda or candy or chocolate or sweets or confection\*** in **Title, Abstract or Keywords** in **all products** | 914 |
| #35 | MeSH descriptor **Carbonated Beverages**, this term only in **MeSH products** | 38 |
| #36 | MeSH descriptor **Cacao**, this term only in **MeSH products** | 65 |
| #37 | MeSH descriptor **Candy**, this term only in **MeSH products** | 31 |
| #38 | (**#7** OR **#8** OR **#9** OR **#10** OR **#11** OR **#12** OR **#13** OR **#14** OR **#15** OR **#16** OR **#17** OR **#18** OR **#19** OR **#20** OR **#21** OR **#22** OR **#23** OR **#24** OR **#25** OR **#26** OR **#27** OR **#28** OR **#29** OR **#30** OR **#31** OR **#32** OR **#33** OR **#34** OR **#35** OR **#36** OR **#37**) | 47367 |
| #39 | (**#6** AND **#38**) | 4175 |
| #40 | MeSH descriptor **Infant Food** explode all trees in **MeSH products** | 818 |
| #41 | MeSH descriptor **Infant Nutrition**, this term only in **MeSH products** | 421 |
| #42 | MeSH descriptor **Child Nutrition**, this term only in **MeSH products** | 169 |
| #43 | **(infant or child) near/3 (food\* or nutrition\* or feed\*)** in **Title, Abstract or Keywords** in **all products** | 2241 |

| #44 | (#40 OR #41 OR #42 OR #43) | 2271 |
|---|---|---|
| #45 | <nothing>, from 1995 to 2006 in all products | 292971 |
| #46 | (#44 AND #45) | 1335 |
| #47 | (#39 OR #46) | 4528 |
| #48 | MeSH descriptor Food Hypersensitivity explode all trees in MeSH products | 386 |
| #49 | food near/3 (allerg* or sensitiv*) in Title, Abstract or Keywords in all products | 256 |
| #50 | MeSH descriptor Dental Caries, this term only in MeSH products | 843 |
| #51 | MeSH descriptor Tooth Loss, this term only in MeSH products | 21 |
| #52 | MeSH descriptor Tooth Erosion, this term only in MeSH products | 57 |
| #53 | dental caries or ((dental or tooth) near/3 (loss or decay or erosion)) in Title, Abstract or Keywords in all products | 1622 |
| #54 | MeSH descriptor Nutritional Status, this term only in MeSH products | 788 |
| #55 | MeSH descriptor Growth, this term only in MeSH products | 547 |
| #56 | MeSH descriptor Body Weight, this term only in MeSH products | 4004 |
| #57 | MeSH descriptor Malnutrition, this term only in MeSH products | 42 |
| #58 | nutritional status or body weight or bodyweight or malnutrition in Title, Abstract or Keywords in all products | 13734 |
| #59 | MeSH descriptor Thinness, this term only in MeSH products | 43 |
| #60 | MeSH descriptor Obesity, this term only in MeSH products | 2948 |
| #61 | overweight or obes* or thinness or (body near/3 (height or size)) in Title, Abstract or Keywords in all products | 6339 |
| #62 | MeSH descriptor Body Height, this term only in MeSH products | 830 |
| #63 | MeSH descriptor Body Size, this term only in MeSH | 31 |

| | | |
|---|---|---|
| | **products** | |
| #64 | MeSH descriptor **Child Development**, this term only in **MeSH products** | 623 |
| #65 | **child\* near/3 (development or growth) in Title, Abstract or Keywords in all products** | 1487 |
| #66 | **breastfeeding near/4 (length or duration) in Title, Abstract or Keywords in all products** | 92 |
| #67 | MeSH descriptor **Rickets**, this term only in **MeSH products** | 24 |
| #68 | **rickets in Title, Abstract or Keywords in all products** | 61 |
| #69 | **(nutrition\* or nutrient\* or micronutrient\* or diet\* or energy) near/3 (intake or advice or counsel\* or education or supplement\* or requirement\* or value) in Title, Abstract or Keywords in all products in All Fields in all products** | 360066 |
| #70 | **MeSH descriptor Energy Intake, this term only in MeSH products in All Fields in all products** | 976 |
| #71 | **MeSH descriptor Nutritive Value, this term only in MeSH products in All Fields in all products** | 976 |
| #72 | **MeSH descriptor Nutritional Requirements, this term only in MeSH products in All Fields in all products** | 976 |
| #73 | **MeSH descriptor Nutritional Requirements, this term only in MeSH products in All Fields in all products** | 976 |
| #74 | MeSH descriptor **Anemia, Iron-Deficiency**, this term only in **MeSH products** | 286 |
| #75 | **anemi\* or aenemi\* or iron deficien\* in Title, Abstract or Keywords in all products** | 3430 |
| #76 | MeSH descriptor **Gastrointestinal Diseases** explode all trees in **MeSH products** | 15511 |
| #77 | MeSH descriptor **Parasitic Diseases** explode all trees in **MeSH products** | 3505 |
| #78 | **(parasitic or gastrointestinal or respiratory) near/3 (disease\* or infection\* or parasite\*) in Title, Abstract or Keywords in all products** | 5059 |
| #79 | MeSH descriptor **Respiratory Tract Diseases** explode all trees in **MeSH products** | 26648 |
| #80 | MeSH descriptor **Asthma**, this term only in **MeSH products** | 6965 |
| #81 | MeSH descriptor **Eczema**, this term only in **MeSH** | 266 |

| | | |
|---|---|---|
| | **products** | |
| #82 | **asthma or eczema or wheeze** in **Title, Abstract or Keywords** in **all products** | 15586 |
| #83 | MeSH descriptor **Mortality**, this term only in **MeSH products** | 262 |
| #84 | MeSH descriptor **Infant Mortality**, this term only in **MeSH products** | 293 |
| #85 | MeSH descriptor **Morbidity**, this term only in **MeSH products** | 535 |
| #86 | **mortality or morbidity** in **Title, Abstract or Keywords** in **all products** | 26064 |
| #87 | MeSH descriptor **Health Knowledge, Attitudes, Practice**, this term only in **MeSH products** | 1360 |
| #88 | **health near/3 (knowledge or attitude\* or practice\*)** in **Title, Abstract or Keywords** in **all products** | 4218 |
| #89 | MeSH descriptor **Maternal Behavior**, this term only in **MeSH products** | 93 |
| #90 | MeSH descriptor **Paternal Behavior**, this term only in **MeSH products** | 4 |
| #91 | **(maternal or paternal or mother\* or father\* or parent\* or carer\*) near/3 (behavior\* or behaviour\* or knowledge or practice\*)** in **Title, Abstract or Keywords** in **all products** | 767 |
| #92 | (**#48** OR **#49** OR **#50** OR **#51** OR **#52** OR **#53** OR **#54** OR **#55** OR **#56** OR **#57** OR **#58** OR **#59** OR **#60** OR **#61** OR **#62** OR **#63** OR **#64** OR **#65** OR **#66** OR **#67** OR **#68** OR **#69** OR **#70** OR **#71** OR **#72** OR **#73** OR **#74** OR **#75** OR **#76** OR **#77** OR **#78** OR **#79** OR **#80** OR **#81** OR **#82** OR **#83** OR **#84** OR **#85** OR **#86** OR **#87** OR **#88** OR **#89** OR **#90** OR **#91**) | 379396 |
| #93 | (**#47** AND **#92**) | 4240 |
| #94 | MeSH descriptor **Developing Countries** explode all trees in **MeSH products** | 414 |
| #95 | MeSH descriptor **Asia** explode all trees in **MeSH products** | 4365 |
| #96 | MeSH descriptor **Africa** explode all trees in **MeSH products** | 2029 |
| #97 | MeSH descriptor **Latin America** explode all trees in **MeSH products** | 46 |
| #98 | MeSH descriptor **South America** explode all trees in **MeSH products** | 641 |

| #99 | MeSH descriptor **Central America** explode all trees in **MeSH products** | 117 |
| #100 | MeSH descriptor **Caribbean Region** explode all trees in **MeSH products** | 170 |
| #101 | (**#94** OR **#95** OR **#96** OR **#97** OR **#98** OR **#99** OR **#100**) | 7363 |
| #102 | (**#93** AND NOT **#101**) | 3594 |

(Hits shown are for all records in Cochrane Library- not just Cochrane reviews. Of the 3594 final hits, 3420 were on the Cochrane Central Register of Clinical Trials)

**(c) translated (including RCT filter) for Cinahl and run for 1990 onwards, excluding developing countries (using MeSH terms), and restricted to English language studies.**

Database: CINAHL - Cumulative Index to Nursing , Allied Health Literature 1982 to April Week 3 2006
1    infant/ or (infant or infants).ti,ab. (44468)
2    child, preschool/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (39697)
3    or/1-2 (62789)
4    limit 3 to (english language and yr="1990 - 2006") (57492)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (15245)
6    (solid food or solids or baby food$).ti,ab. (193)
7    weaning/ or (wean$ or weaning).ti,ab. (1407)
8    family food.ti,ab. (14)
9    exp fruit/ or vegetables/ or fruit$.ti,ab. or vegetable$.ti,ab. (4135)
10    sodium.ti,ab. (1938)
11    sodium chloride, dietary/ (390)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (10286)
13    minerals.ti,ab. or exp minerals/ (1493)
14    food habits/ or exp food/ or nutrition/ or nutrition policy/ (24918)
15    health behavior/ or diet/ or eating behavior/ (17793)
16    ((nutrition$ or nutrient$ or nutritive or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutrients/ (9778)
17    (nutrition$ adj3 knowledge).ti,ab. (281)
18    breastfeeding.ti,ab. or breastfeeding/ (5978)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or candy/ (981)
20    or/5-19 (66503)
21    4 and 20 (7222)
22    exp infant feeding/ or infant food/ or infant nutrition/ or (infant adj3 (food$ or nutrition or feed$)).ti,ab. (7263)
23    child nutrition/ or (child$ adj3 (food$ or nutrition or feed$)).ti,ab. (2535)
24    or/22-23 (9470)
25    limit 24 to (english language and yr="1990 - 2006") (8510)
26    21 or 25 (11885)
27    exp food hypersensitivity/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (1113)

28   exp dental caries/ or dental caries.ti,ab. or tooth loss/ or tooth erosion/ or (tooth adj4 (loss or erosion or decay)).ti,ab. (1981)
29   nutritional status/ or nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body weight changes/ or weight.ti,ab. or bodyweight.ti,ab. or nutrition disorders/ or malnutrition.ti,ab. (30433)
30   obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness/ or thinness.ti,ab. or body height/ or (body adj4 (height or size)).ti,ab. (12078)
31   child development/ or (child$ adj3 (development or growth)).ti,ab. (5163)
32   (breastfeeding adj3 (length or duration)).ti,ab. (301)
33   rickets/ or rickets.ti,ab. (137)
34   ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutrients/ (7702)
35   (anemi$ or anaemi$).ti,ab. or anemia, iron deficiency/ or iron deficien$.ti,ab. (2580)
36   exp gastrointestinal diseases/ (15478)
37   exp parasitic diseases/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (7318)
38   exp respiratory tract infections/ (12393)
39   Asthma/ or (asthma or wheeze).ti,ab. (9279)
40   Eczema/ or eczema.ti,ab. (687)
41   mortality/ or infant mortality/ or child mortality/ or mortality.ti,ab. (19340)
42   Morbidity/ or morbidity.ti,ab. (9922)
43   exp attitude to health/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (30607)
44   exp family attitudes/ or maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (7921)
45   paternal behavior/ (40)
46   or/27-45 (143309)
47   26 and 46 (5403)
48   exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (38475)
49   developing countries/ (2428)
50   or/48-49 (40389)
51   47 not 50 (4578)
52   exp clinical trials/ (36679)
53   double blind studies/ (7302)
54   single-blind studies/ (1911)
55   triple-blind studies/ (31)
56   clinical trial.pt. (17004)
57   random assignment/ (12464)
58   (randomized or randomised or placebo or randomly).ab. (27422)
59   trial.ti. (8600)
60   or/52-59 (54501)
61   51 and 60 (541)
62   animals/ not (animals/ and humans/) (610)
63   61 not 62 (541)
64   from 63 keep 1-541 (541)


**(d) translated (including RCT filter) for EMBASE and run for 1990 onwards, excluding developing countries (using MeSH terms), and restricted to English language studies.**

Database: EMBASE 1980 to 2006 Week 16

1    infant/ or (infant or infants).ti,ab. (219518)
2    preschool child/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (95474)
3    or/1-2 (283860)
4    limit 3 to (english language and yr="1990 - 2006") (178266)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (57721)
6    (solid food or solids or baby food$).ti,ab. (10288)
7    weaning/ or (wean$ or weaning).ti,ab. (16460)
8    family food.ti,ab. (46)
9    exp fruit/ or vegetable/ or fruit$.ti,ab. or vegetable$.ti,ab. (33632)
10    sodium.ti,ab. (156325)
11    exp electrolyte intake/ (7893)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamin/ (251178)
13    minerals.ti,ab. or exp nutrients/ or mineral intake/ (6353)
14    exp food/ or exp nutrition/ (683161)
15    health behavior/ or diet/ or feeding behavior/ (66291)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or dietary intake/ (64378)
17    (nutrition$ adj3 knowledge).ti,ab. (696)
18    breastfeeding.ti,ab. or breastfeeding/ (3147)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or sugar/ (13146)
20    or/5-19 (940481)
21    4 and 20 (24576)
22    exp infant nutrition/ or (infant adj3 (food$ or nutrition)).ti,ab. (20687)
23    child nutrition/ or (child$ adj3 (food$ or nutrition)).ti,ab. (5372)
24    or/22-23 (25259)
25    limit 24 to (english language and yr="1990 - 2006") (18026)
26    21 or 25 (33292)
27    exp food allergy/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (8192)
28    exp tooth disease/ or dental caries.ti,ab. or (tooth adj2 (loss or erosion or decay)).ti,ab. (20726)
29    nutritional status/ or nutritional status.ti,ab. or body weight/ or weight.ti,ab. or bodyweight.ti,ab. or exp nutritional disorder/ or malnutrition.ti,ab. (432600)
30    obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness.ti,ab. or (body adj2 (height or size)).ti,ab. (84535)
31    child development/ or (child$ adj3 (development or growth)).ti,ab. (23840)
32    (breastfeeding adj3 (length or duration)).ti,ab. (470)
33    rickets/ or rickets.ti,ab. (2847)
34    ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or dietary intake/ (52299)
35    (anemi$ or anaemi$).ti,ab. or iron deficiency anemia,/ or iron deficien$.ti,ab. (49971)
36    gastrointestinal disease/ (12810)
37    parasitosis/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (47022)
38    respiratory tract disease/ (12936)
39    Asthma/ or (asthma or wheeze).ti,ab. (78177)
40    Eczema/ or eczema.ti,ab. (9163)
41    infant mortality/ or child mortality/ (5849)
42    Morbidity/ or morbidity.ti,ab. (128234)

43    (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (10231)
44    maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (11462)
45    paternal behavior/ (488)
46    or/27-45 (818823)
47    26 and 46 (16565)
48    exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (205246)
49    developing countries/ (16894)
50    or/48-49 (216435)
51    47 not 50 (13576)
52    controlled study/ (2151388)
53    exp clinical trial/ (385764)
54    outcomes research/ (54972)
55    randomized controlled trial/ (104939)
56    (randomized or randomised or randomly or placebo).ab. (270650)
57    trial.ti. (52353)
58    or/52-57 (2468183)
59    51 and 58 (5753)
60    animal/ not (animal/ and human/) (12808)
61    59 not 60 (5753)
62    from 61 keep 1-5753 (5753)

**(e) translated (including RCT filter) for PsycINFO and run for 1990 onwards, excluding developing countries (using MeSH terms), and restricted to English language studies.**

Database: PsycINFO 1985 to April Week 4 2006
1    exp infant development/ or (infant or infants).ti,ab. (26351)
2    (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (19889)
3    or/1-2 (44856)
4    limit 3 to (english language and yr="1990 - 2006") (31308)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (26875)
6    (solid food or solids or baby food$).ti,ab. (207)
7    weaning/ or (wean$ or weaning).ti,ab. (1585)
8    family food.ti,ab. (27)
9    (fruit$ or vegetable$).ti,ab. (3974)
10    sodium.ti,ab. (2547)
11    sodium/ (890)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (2636)
13    minerals.ti,ab. (150)
14    food preferences/ or exp food/ or exp nutrition/ or food intake/ (10183)
15    eating behavior/ or exp diets/ (4960)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy expenditure/ (4564)
17    (nutrition$ adj3 knowledge).ti,ab. (224)
18    breastfeeding.ti,ab. or exp breastfeeding/ (581)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. (884)
20    or/5-19 (48617)

21    4 and 20 (1338)
22    (infant adj3 (food$ or nutrition)).ti,ab. (64)
23    (child$ adj3 (food$ or nutrition)).ti,ab. (628)
24    or/22-23 (680)
25    limit 24 to (english language and yr="1990 - 2006") (566)
26    21 or 25 (1784)
27    exp food allergies/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (189)
28    (dental caries or (tooth adj4 (loss or erosion or decay))).ti,ab. (64)
29    nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body size/ or weight.ti,ab. or bodyweight.ti,ab. or nutritional deficiencies/ or malnutrition.ti,ab. (42288)
30    exp obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness.ti,ab. or (body adj4 (height or size)).ti,ab. (8989)
31    child development/ or early childhood development/ or (child$ adj3 (development or growth)).ti,ab. (21313)
32    (breastfeeding adj3 (length or duration)).ti,ab. (97)
33    rickets.ti,ab. (10)
34    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy expenditure/ (4564)
35    (anemi$ or anaemi$).ti,ab. or anemia/ or iron deficien$.ti,ab. (503)
36    exp gastrointestinal disorders/ (2691)
37    exp parasitic disorders/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (913)
38    exp respiratory tract disorders/ (4347)
39    Asthma/ or (asthma or wheeze).ti,ab. (2161)
40    Eczema/ or eczema.ti,ab. (91)
41    mortality rate/ or mortality.ti,ab. (8243)
42    morbidity.ti,ab. (6428)
43    health knowledge, attitudes, practice/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (6579)
44    mother child relations/ or mother child communication/ or parent child relations/ or parent child communication/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (38558)
45    father child relations/ or father child communication/ (2466)
46    or/27-45 (128746)
47    26 and 46 (1022)
48    exp developing countries/ or exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (20525)
49    47 not 48 (990)
50    (empirical study or quantitative study).md. (830270)
51    treatment outcome clinical trial.md. (10357)
52    experimental design/ (4221)
53    (randomized or placebo or randomly).ab. (39678)
54    trial.ti. (5491)
55    or/50-54 (839684)
56    49 and 55 (718)
57    animals/ not (animals/ and humans/) (2278)
58    56 not 57 (718)
59    from 58 keep 1-718 (718)


The search results from all searches were downloaded into an Endnote library and deduplicated.

| Search | Results/Imported | Results after deduplication | Custom4 code |
|---|---|---|---|
| RCT medline | 2511 | 1654 | medline rct child nutrition |
| RCT central | 3420 | 807 | central rct child nutrition |
| RCT cinahl | 541 | 177 | cinahl rct child nutrition |
| RCT embase | 5753 | 2886 | embase rct child nutrition |
| RCT psycinfo | 718 | 413 | psycinfo rct child nutrition |

## UK Studies (not RCTs) (17/03/06)

The search strategies used for the RCT searches of Medline, Embase, Cinahl and Psycinfo were repeated, but RCTs and reviews were excluded, and the searches limited to UK only or studies by UK institutions.

**Database: Ovid MEDLINE(R) <1966 to April Week 3 2006>**
1    infant/ or (infant or infants).ti,ab. (544028)
2    child, preschool/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (567032)
3    or/1-2 (813397)
4    limit 3 to (english language and yr="1990 - 2006") (337550)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (68072)
6    (solid food or solids or baby food$).ti,ab. (6305)
7    weaning/ or (wean$ or weaning).ti,ab. (24735)
8    family food.ti,ab. (64)
9    exp fruit/ or vegetables/ or fruit$.ti,ab. or vegetable$.ti,ab. (53926)
10    sodium, dietary/ or sodium.ti,ab. (186306)
11    sodium chloride, dietary/ (1858)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (259600)
13    minerals.ti,ab. or exp minerals/ (69562)
14    food habits/ or exp food/ or nutrition/ or nutrition policy/ (451147)
15    health behavior/ or diet/ or feeding behavior/ (102527)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutritive value/ (79802)
17    (nutrition$ adj3 knowledge).ti,ab. (717)
18    breastfeeding.ti,ab. or breastfeeding/ (18800)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or candy/ (10205)
20    or/5-19 (1069244)
21    4 and 20 (30858)
22    infant food/ or infant nutrition/ or (infant adj3 (food$ or nutrition)).ti,ab. (15242)
23    child nutrition/ or (child$ adj3 (food$ or nutrition)).ti,ab. (7510)
24    or/22-23 (21592)
25    limit 24 to (english language and yr="1990 - 2006") (8756)

26    21 or 25 (33704)
27    exp food hypersensitivity/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (10200)
28    exp dental caries/ or dental caries.ti,ab. or tooth loss/ or tooth erosion/ or (tooth adj4 (loss or erosion or decay)).ti,ab. (31122)
29    nutritional status/ or nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body weight changes/ or weight.ti,ab. or bodyweight.ti,ab. or malnutrition/ or malnutrition.ti,ab. (944319)
30    overweight/ or overweight.ti,ab. or obes$.ti,ab. or thinness/ or thinness.ti,ab. or body height/ or body size/ or (body adj4 (height or size)).ti,ab. (105314)
31    child development/ or (child$ adj3 (development or growth)).ti,ab. (34873)
32    (breastfeeding adj3 (length or duration)).ti,ab. (719)
33    rickets/ or rickets.ti,ab. (5073)
34    ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutritive value/ (67225)
35    (anemi$ or anaemi$).ti,ab. or anemia, iron deficiency/ or iron deficien$.ti,ab. (69682)
36    exp gastrointestinal diseases/ (494192)
37    exp parasitic diseases/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (247196)
38    exp respiratory tract diseases/ (690651)
39    Asthma/ or (asthma or wheeze).ti,ab. (85689)
40    Eczema/ or eczema.ti,ab. (9424)
41    mortality/ or infant mortality/ or mortality.ti,ab. (247406)
42    Morbidity/ or morbidity.ti,ab. (128904)
43    health knowledge, attitudes, practice/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (39326)
44    maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (13639)
45    paternal behavior/ (884)
46    or/27-45 (2679767)
47    26 and 46 (19561)
48    exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (439496)
49    developing countries/ (45951)
50    or/48-49 (456371)
51    47 not 50 (15364)
52    clinical trial.pt. (428181)
53    (randomized or placebo).ab. or clinical trials/ (300865)
54    randomly.ab. or trial.ti. (151868)
55    or/52-54 (607054)
56    51 not 55 (12790)
57    animals/ not (animals/ and humans/) (2962375)
58    56 not 57 (12398)
59    exp great britain/ (208103)
60    (united kingdom or great britain or england or wales or scotland or ireland).in. (182658)
61    or/59-60 (380175)
62    58 and 61 (744)
63    from 62 keep 1-744 (744)


**Database: CINAHL - Cumulative Index to Nursing , Allied Health Literature <1982 to April Week 3 2006>**
1    infant/ or (infant or infants).ti,ab. (44468)

2     child, preschool/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (39697)
3     or/1-2 (62789)
4     limit 3 to (english language and yr="1990 - 2006") (57492)
5     ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (15245)
6     (solid food or solids or baby food$).ti,ab. (193)
7     weaning/ or (wean$ or weaning).ti,ab. (1407)
8     family food.ti,ab. (14)
9     exp fruit/ or vegetables/ or fruit$.ti,ab. or vegetable$.ti,ab. (4135)
10    sodium.ti,ab. (1938)
11    sodium chloride, dietary/ (390)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (10286)
13    minerals.ti,ab. or exp minerals/ (1493)
14    food habits/ or exp food/ or nutrition/ or nutrition policy/ (24918)
15    health behavior/ or diet/ or eating behavior/ (17793)
16    ((nutrition$ or nutrient$ or nutritive or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutrients/ (9778)
17    (nutrition$ adj3 knowledge).ti,ab. (281)
18    breastfeeding.ti,ab. or breastfeeding/ (5978)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or candy/ (981)
20    or/5-19 (66503)
21    4 and 20 (7222)
22    exp infant feeding/ or infant food/ or infant nutrition/ or (infant adj3 (food$ or nutrition or feed$)).ti,ab. (7263)
23    child nutrition/ or (child$ adj3 (food$ or nutrition or feed$)).ti,ab. (2535)
24    or/22-23 (9470)
25    limit 24 to (english language and yr="1990 - 2006") (8510)
26    21 or 25 (11885)
27    exp food hypersensitivity/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (1113)
28    exp dental caries/ or dental caries.ti,ab. or tooth loss/ or tooth erosion/ or (tooth adj4 (loss or erosion or decay)).ti,ab. (1981)
29    nutritional status/ or nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body weight changes/ or weight.ti,ab. or bodyweight.ti,ab. or nutrition disorders/ or malnutrition.ti,ab. (30433)
30    obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness/ or thinness.ti,ab. or body height/ or (body adj4 (height or size)).ti,ab. (12078)
31    child development/ or (child$ adj3 (development or growth)).ti,ab. (5163)
32    (breastfeeding adj3 (length or duration)).ti,ab. (301)
33    rickets/ or rickets.ti,ab. (137)
34    ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or energy intake/ or nutritional requirements/ or nutrients/ (7702)
35    (anemi$ or anaemi$).ti,ab. or anemia, iron deficiency/ or iron deficien$.ti,ab. (2580)
36    exp gastrointestinal diseases/ (15478)
37    exp parasitic diseases/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (7318)
38    exp respiratory tract infections/ (12393)
39    Asthma/ or (asthma or wheeze).ti,ab. (9279)
40    Eczema/ or eczema.ti,ab. (687)

41    mortality/ or infant mortality/ or child mortality/ or mortality.ti,ab. (19340)
42    Morbidity/ or morbidity.ti,ab. (9922)
43    exp attitude to health/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (30607)
44    exp family attitudes/ or maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (7921)
45    paternal behavior/ (40)
46    or/27-45 (143309)
47    26 and 46 (5403)
48    exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (38475)
49    developing countries/ (2428)
50    or/48-49 (40389)
51    47 not 50 (4578)
52    exp clinical trials/ (36679)
53    double blind studies/ (7302)
54    single-blind studies/ (1911)
55    triple-blind studies/ (31)
56    clinical trial.pt. (17004)
57    random assignment/ (12464)
58    (randomized or randomised or placebo or randomly).ab. (27422)
59    trial.ti. (8600)
60    or/52-59 (54501)
61    51 not 60 (4037)
62    animals/ not (animals/ and humans/) (610)
63    61 not 62 (4030)
64    exp united kingdom/ or (united kingdom or great britain or uk or england or wales or scotland or ireland).in. (124156)
65    63 and 64 (477)
66    from 65 keep 1-477 (477)

**Database: EMBASE <1980 to 2006 Week 16>**
1    infant/ or (infant or infants).ti,ab. (219518)
2    preschool child/ or (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (95474)
3    or/1-2 (283860)
4    limit 3 to (english language and yr="1990 - 2006") (178266)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (57721)
6    (solid food or solids or baby food$).ti,ab. (10288)
7    weaning/ or (wean$ or weaning).ti,ab. (16460)
8    family food.ti,ab. (46)
9    exp fruit/ or vegetable/ or fruit$.ti,ab. or vegetable$.ti,ab. (33632)
10    sodium.ti,ab. (156325)
11    exp electrolyte intake/ (7893)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamin/ (251178)
13    minerals.ti,ab. or exp nutrients/ or mineral intake/ (6353)
14    exp food/ or exp nutrition/ (683161)
15    health behavior/ or diet/ or feeding behavior/ (66291)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or dietary intake/ (64378)
17    (nutrition$ adj3 knowledge).ti,ab. (696)

18    breastfeeding.ti,ab. or breastfeeding/ (3147)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. or carbonated beverages/ or cacao/ or sugar/ (13146)
20    or/5-19 (940481)
21    4 and 20 (24576)
22    exp infant nutrition/ or (infant adj3 (food$ or nutrition)).ti,ab. (20687)
23    child nutrition/ or (child$ adj3 (food$ or nutrition)).ti,ab. (5372)
24    or/22-23 (25259)
25    limit 24 to (english language and yr="1990 - 2006") (18026)
26    21 or 25 (33292)
27    exp food allergy/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (8192)
28    exp tooth disease/ or dental caries.ti,ab. or (tooth adj2 (loss or erosion or decay)).ti,ab. (20726)
29    nutritional status/ or nutritional status.ti,ab. or body weight/ or weight.ti,ab. or bodyweight.ti,ab. or exp nutritional disorder/ or malnutrition.ti,ab. (432600)
30    obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness.ti,ab. or (body adj2 (height or size)).ti,ab. (84535)
31    child development/ or (child$ adj3 (development or growth)).ti,ab. (23840)
32    (breastfeeding adj3 (length or duration)).ti,ab. (470)
33    rickets/ or rickets.ti,ab. (2847)
34    ((nutrition$ or nutritive or nutrient$ or micronutrient$ or dietary or energy) adj3 (intake or status or value)).ti,ab. or dietary intake/ (52299)
35    (anemi$ or anaemi$).ti,ab. or iron deficiency anemia,/ or iron deficien$.ti,ab. (49971)
36    gastrointestinal disease/ (12810)
37    parasitosis/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (47022)
38    respiratory tract disease/ (12936)
39    Asthma/ or (asthma or wheeze).ti,ab. (78177)
40    Eczema/ or eczema.ti,ab. (9163)
41    infant mortality/ or child mortality/ (5849)
42    Morbidity/ or morbidity.ti,ab. (128234)
43    (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (10231)
44    maternal behavior/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (11462)
45    paternal behavior/ (488)
46    or/27-45 (818823)
47    26 and 46 (16565)
48    exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (205246)
49    developing countries/ (16894)
50    or/48-49 (216435)
51    47 not 50 (13576)
52    controlled study/ (2151388)
53    exp clinical trial/ (385764)
54    outcomes research/ (54972)
55    randomized controlled trial/ (104939)
56    (randomized or randomised or randomly or placebo).ab. (270650)
57    trial.ti. (52353)
58    or/52-57 (2468183)
59    51 not 58 (7823)
60    animal/ not (animal/ and human/) (12808)
61    59 not 60 (7823)

62    united kingdom/ or (united kingdom or uk or england or wales or scotland or ireland or great britain).in. (863816)
63    61 and 62 (1023)
64    from 63 keep 1-1023 (1023)


**Database: PsycINFO <1985 to April Week 4 2006>**

1    exp infant development/ or (infant or infants).ti,ab. (26351)
2    (preschool$ or nurser$ or playschool$ or kindergarten$ or creche$ or (pre adj school$)).ti,ab. (19889)
3    or/1-2 (44856)
4    limit 3 to (english language and yr="1990 - 2006") (31308)
5    ((food or nutrition$ or diet$ or nutritive or feed$ or eating or health) adj3 (supplement$ or habit$ or behavior$ or behaviour$ or attitude$ or belief$ or polic$ or value)).ti,ab. (26875)
6    (solid food or solids or baby food$).ti,ab. (207)
7    weaning/ or (wean$ or weaning).ti,ab. (1585)
8    family food.ti,ab. (27)
9    (fruit$ or vegetable$).ti,ab. (3974)
10    sodium.ti,ab. (2547)
11    sodium/ (890)
12    (vitamin or vitamins or iron).ti,ab. or exp vitamins/ (2636)
13    minerals.ti,ab. (150)
14    food preferences/ or exp food/ or exp nutrition/ or food intake/ (10183)
15    eating behavior/ or exp diets/ (4960)
16    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy expenditure/ (4564)
17    (nutrition$ adj3 knowledge).ti,ab. (224)
18    breastfeeding.ti,ab. or exp breastfeeding/ (581)
19    (((salt or sugar) adj3 (intake or consumption)) or soft drinks or soda or candy or chocolate or sweets or confection$).ti,ab. (884)
20    or/5-19 (48617)
21    4 and 20 (1338)
22    (infant adj3 (food$ or nutrition)).ti,ab. (64)
23    (child$ adj3 (food$ or nutrition)).ti,ab. (628)
24    or/22-23 (680)
25    limit 24 to (english language and yr="1990 - 2006") (566)
26    21 or 25 (1784)
27    exp food allergies/ or (food adj3 (allerg$ or sensitivit$)).ti,ab. (189)
28    (dental caries or (tooth adj4 (loss or erosion or decay))).ti,ab. (64)
29    nutritional status.ti,ab. or growth/ or growth.ti,ab. or body weight/ or body size/ or weight.ti,ab. or bodyweight.ti,ab. or nutritional deficiencies/ or malnutrition.ti,ab. (42288)
30    exp obesity/ or overweight.ti,ab. or obes$.ti,ab. or thinness.ti,ab. or (body adj4 (height or size)).ti,ab. (8989)
31    child development/ or early childhood development/ or (child$ adj3 (development or growth)).ti,ab. (21313)
32    (breastfeeding adj3 (length or duration)).ti,ab. (97)
33    rickets.ti,ab. (10)
34    ((nutrition$ or nutrient$ or micronutrient$ or diet$ or energy) adj3 (intake or advice or counsel$ or education or supplement$ or requirement$ or value)).ti,ab. or energy expenditure/ (4564)
35    (anemi$ or anaemi$).ti,ab. or anemia/ or iron deficien$.ti,ab. (503)
36    exp gastrointestinal disorders/ (2691)

37    exp parasitic disorders/ or ((parasitic or gastrointestinal or respiratory) adj3 (disease$ or infection$ or parasite$)).ti,ab. (913)
38    exp respiratory tract disorders/ (4347)
39    Asthma/ or (asthma or wheeze).ti,ab. (2161)
40    Eczema/ or eczema.ti,ab. (91)
41    mortality rate/ or mortality.ti,ab. (8243)
42    morbidity.ti,ab. (6428)
43    health knowledge, attitudes, practice/ or (health adj3 (knowledge or practice$ or attitude$)).ti,ab. (6579)
44    mother child relations/ or mother child communication/ or parent child relations/ or parent child communication/ or ((maternal or paternal or mother$ or father$ or parent$ or carer$) adj3 (behavior$ or behaviour$ or knowledge or attitude$ or belief$ or practice$)).ti,ab. (38558)
45    father child relations/ or father child communication/ (2466)
46    or/27-45 (128746)
47    26 and 46 (1022)
48    exp developing countries/ or exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp south america/ or exp asia/ (20525)
49    47 not 48 (990)
50    (empirical study or quantitative study).md. (830270)
51    treatment outcome clinical trial.md. (10357)
52    experimental design/ (4221)
53    (randomized or placebo or randomly).ab. (39678)
54    trial.ti. (5491)
55    or/50-54 (839684)
56    49 not 55 (272)
57    animals/ not (animals/ and humans/) (2278)
58    56 not 57 (271)
59    (britain or united kingdom).lo. (15410)
60    (united kingdom or uk or england or wales or scotland or ireland or great britain).in. (128302)
61    or/59-60 (130706)
62    58 and 61 (43)
63    from 62 keep 1-43 (43)

**Results of UK searches**
The search results from all searches were downloaded into an Endnote library and then deduplicated.

| Search | Results | After deduplication | Custom4 code |
|---|---|---|---|
| medline uk | 744 | 488 | medline uk child nutrition |
| cinahl uk | 477 | 412 | cinahl uk child nutrition |
| embase uk | 1021 | 748 | embase uk child nutrition |
| psycinfo uk | 43 | 33 | psycinfo uk child nutrition |

## Update searches

**Maternal and child nutrition: update searches**
**Julie Glanville**
**30 January 2007**

Where possible the original saved searches were rerun. Where saved searches were not available the original search strategies as recorded in the original search writeup were retyped into the relevant database/search engines.

<u>Nutrition of children aged 7 months to 5 years - reviews, RCTs and UK studies</u>

| Database | Records retrieved | Records after deduplication against update searches and original library |
|---|---|---|
| **Reviews** | | |
| CDSR (Cochrane Library 2006/2; 2006/3 and 2006/4) | 100 | 96 |
| DARE (CRD admin database) | 22 | 0 |
| NRR (issue 2006/1; 2006/2; 2006/3 and 2006/4) | 100 | 92 |
| HTA (CRD admin database 17/1/07) | 0 | 0 |
| SIGN (SIGN website) | 0 | 0 |
| NGC (NGC website) | 2 | 1 |
| NCCHTA (NCCHTA website) | 0 | 0 |
| NICE (NICE website) | 0 | 0 |
| HSTAT (HSTAT interface) | 0 | 0 |
| ReFeR (ReFeR website) | 0 | 0 |
| TRIP (TRIP website) | 0 | 0 |
| Clinical evidence | 0 | 0 |
| HEBW (website) | 0 | 0 |
| | | **Total new citations (reviews) = 189** |
| **RCTs** | | |
| Medline (Ovid, 17/1/07) | 142 | 89 |
| Central (Cochrane Library 2006/2; 2006/3 and 2006/4) | 356 | 294 |
| Cinahl (Ovid, 16/1/07) | 154 | 20 |
| Embase (Ovid, 17/1/07) | 874 | 432 |
| Psycinfo (Ovid, 30/1/07) | 100 | 59 |
| | | **Total new citations (RCTs) = 894** |
| **UK** | | |
| Medline (Ovid, 17/1/07) | 61 | 53 |
| Cinahl (Ovid, 16/1/07) | 81 | 47 |
| Embase (Ovid, 17/1/07) | 73 | 46 |
| Psycinfo (Ovid, 30/1/07) | 4 | 4 |
| | | **Total new citations (UK studies) = 150** |

# APPENDIX D – Methodology checklist

From: National Institute for Health and Clinical Excellence (2006). *Methods for development of NICE public health guidance.* London: National Institute for Health and Clinical Excellence. Available from:

## Notes on the use of methodology checklist: systematic reviews

**Section 1** identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review – that is, making sure that it has been carried out carefully, and that the outcomes are likely to be attributable to the intervention being investigated. Each question covers an aspect of methodology that research has shown makes a significant difference to the conclusions of a study. For each question in this section you should use one of the following to indicate how well it has been addressed in the review.

Well covered

Adequately addressed

Poorly addressed

Not addressed (that is, not mentioned, or indicates that this aspect of study design was ignored)

Not reported (that is, mentioned, but insufficient detail to allow assessment to be made)

Not applicable

### The study addresses an appropriate and clearly focused question

Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

### A description of the methodology used is included

One of the key distinctions between a systematic review and a general review is the systematic methodology used. A systematic review should include a detailed description of the methods used to identify and evaluate individual studies. If this description is not present, it is not possible to make a thorough evaluation of the quality of the review, and **it should be rejected as a source of level 1 evidence** (though it may be useable as level 4 evidence, if not better evidence can be found).

### The literature search is sufficiently rigorous to identify all the relevant studies

A systematic review based on a limited literature search – for example, one limited to Medline only – is likely to be heavily biased. A well-conducted review should as a minimum look at Embase and Medline, and from the late 1990s onward, the Cochrane Library. Any indication that hand searching of

key journals, or follow up of reference lists of included studies were carried out in addition to electronic database searches can normally be taken as evidence of a well-conducted review.

**Study quality is assessed and taken into account**

A well-conducted systematic review should have used clear criteria to assess whether individual studies had been well conducted before deciding whether to include or exclude them. If there is not indication of such an assessment, **the review should be rejected as a source of level 1 evidence**. If details of the assessment are poor, or the methods are considered to be inadequate, the quality of the review should be downgraded. In either case, it may be worthwhile obtaining and evaluating the individual studies as part of the review you are conducting for this guideline.

**There are enough similarities between the studies selected to make combining them reasonable**

Studies covered by a systematic review should be selected using clear inclusion criteria. These criteria should include, either implicitly or explicitly, the question of whether the selected studies can legitimately be compared. It should be clearly ascertained, for example, that the populations covered by the studies are comparable, that the methods used in the investigations are the same, that the outcome measures are comparable and the variability in effect sized between studies is not greater than would be expected by chance alone.

**Section 2** relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

| ++ | All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter. |
|---|---|
| + | Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions. |
| – | Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter. |

The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.
The aim of the other two questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

**Methodology checklist for systematic reviews**

**First author/year**

**Section 1: Internal validity**

| | **In a well-conducted SR:** | **In this study this criterion is: (copy one option into your column with comment if required)** | Reviewer 1 (initials) | Reviewer 2 (initials) |
|---|---|---|---|---|
| 1.1 | The study addresses an appropriate and clearly focused question | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | |
| 1.2 | A description of the methodology used is included. | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | |
| 1.3 | The literature search is sufficiently rigorous to identify all the relevant studies. | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | |
| 1.4 | Study quality is assessed and taken into account. | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | |
| 1.5 | There are enough similarities between the studies selected to make combining them reasonable. | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | |

**Section 2: Overall assessment of the study**

| | | Reviewer 1 (initials) Comment if desired | Reviewer 2 (initials) Comment if desired | Reviewer 3 (initials) Agreed |
|---|---|---|---|---|
| 2.1 | How well was the study done to minimise bias?<br>Code ++, + or - | | | |
| 2.2 | If coded as + or – what is the likely direction in which bias might affect the study results? | | | |
| 2.3 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain the overall effect is due to the study intervention? | | | |
| 2.4 | Are the results of this study directly applicable to the patient group targeted by this guideline? | | | |

**Notes on the use of methodology checklist: randomised controlled trials**

**Section 1** identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review – that is, making sure that it has been carried out carefully, and that the outcomes are likely to be attributable to the intervention being investigated. Each question covers an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.
For each question in this section you should use one of the following to indicate how well it has been addressed in the study.
Well covered
Adequately addressed
Poorly addressed
Not addressed (that is, not mentioned, or indicates that this aspect of study design was ignored)
Not reported (that is, mentioned, but insufficient detail to allow assessment to be made)
Not applicable

**The study addresses an appropriate and clearly focused question**

Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

**The assignment of subjects to treatment groups is randomised.**

Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study. **If there is no indication of randomisation, the study should be rejected.** If the description of randomisation is poor, or the process used is not truly random (for example, allocation by date, alternating between one group and another) or can otherwise be seen as flawed, the study should be given a lower quality rating.

**An adequate concealment method is used.**

Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%. Centralised allocation, computerised allocation systems or the use of coded identical containers would all be regarded as adequate methods of concealment, and may be taken as indicators of a well-conducted study. If the method of concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating, and can be rejected if the concealment method is seen as inadequate.B.2.4Subjects and investigators are kept 'blind' about treatment allocation.
Blinding can be carried out up to three levels. In single-blind studies, patients are unaware of which treatment they are receiving; in double-blind studies the doctor and the patient are unaware of which treatment the patient is receiving; in triple-blind studies patients, healthcare providers and those conducting the analysis are unaware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

**The treatment and control groups are similar at the start of the trial.**
Patients selected for inclusion in a trial should be as similar as possible, in order to eliminate any possible bias. The study should report any significant differences in the

composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin or comorbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

**The only difference between groups is the treatment under investigation.**

If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were *not* treated equally, the study should be rejected unless no other evidence is available.** If the study *is* used as evidence it should be treated with caution, and given a low quality rating.

**All relevant outcomes measured in a standard, valid and reliable way.**

If some significant clinical outcomes have been ignored, or not adequately taken into account, the study should be downgraded. It should also be downgraded if the measures used are regarded as being doubtful in any way, or applied inconsistently.

**What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?**

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but this may vary. Some regard should be paid to *why* patients dropped out, as well as how many. It should be noted that the drop-out rate may be expected to be higher in studies conducted over a long period of time. A higher drop-out rate will normally lead to downgrading, rather than rejection of a study.

**All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**

In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes *must* be analysed according to the group to which they were originally allocated, irrespective of the treatment they actually received. (This is known as *intention-to-treat* analysis.) If it is clear that analysis was not on an intention-to-treat basis, the quality of the study should be downgraded.

**Where the study is carried out at more then one site, results are comparable for all sites.**

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

**Section 2** relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

| ++ | All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter. |
|---|---|

| ++ | All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter. |
|---|---|
| + | Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions. |
| – | Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter. |

The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.

The aim of the other two questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

**Methodology checklist for RCTs**

**First author/year**

**Section 1: Internal validity**

|  | **In a well-conducted RCT study:** | **In this study this criterion is: (copy one option into your column with comment if required)** | Reviewer 1 (initials) | Reviewer 2 (initials) |
|---|---|---|---|---|
| 1.1 | The study addresses an appropriate and clearly focused question | Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable |  |  |
| 1.2 | The assignment of subjects to treatment groups is randomised | Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable |  |  |
| 1.3 | An adequate concealment method is used | Well covered Adequately addressed Poorly addressed Not addressed Not reported Not applicable |  |  |
| 1.4 | Subjects and investigators are kept 'blind' about treatment allocation | Well covered Adequately addressed Poorly addressed Not addressed Not reported |  |  |

| | | | | | |
|---|---|---|---|---|---|
| | | Not applicable | | | |
| 1.5 | The treatment and control groups are similar at the start of the trial | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | | |
| 1.6 | The only difference between groups is the treatment under investigation | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | | |
| 1.7 | All relevant outcomes are measured in a standard, valid way | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | | |
| 1.8 | What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? | Where available, Reviewer 1 report and Reviewer 2 check:<br>Number randomised into each arm<br>Number in each arm with outcome data at the end of the trial<br>Dropout rate (%) for each arm<br>Dropout rate (%) overall | | | |
| 1.9 | All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis, ITT) | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | | |
| 1.10 | Where the study is carried out at more than one site, results are comparable for all sites | Well covered<br>Adequately addressed<br>Poorly addressed<br>Not addressed<br>Not reported<br>Not applicable | | | |

## Section 2: Overall assessment of the study

| 2.1 | How well was the study done to minimise bias?<br>Code ++, + or - | Reviewer 1 (initials)<br>Comment if desired | Reviewer 2 (initials)<br>Comment if desired | (Reviewer 3)<br>Agreed |
|---|---|---|---|---|
| 2.2 | If coded as + or – what is the likely direction in which bias might affect the study results? | | | |
| 2.3 | Taking into account clinical considerations, your evaluation of | | | |

| | | | | |
|---|---|---|---|---|
| | the methodology used, and the statistical power of the study, are you certain the overall effect is due to the study intervention? | | | |
| 2.4 | Are the results of this study directly applicable to the patient group targeted by this guideline? | | | |