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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Examining the Cost-Effectiveness of Moving the Healthy Start Vitamin Programme from a Targeted to a Universal Offering: Cost-Effectiveness Systematic Review

Final Report

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Executive Summary

1. BACKGROUND

In 2012, the Annual Report of the Chief Medical Officer ("Our children deserve better – Prevention pays") highlighted the importance of vitamin supplementation in mothers and young children and the growing concerns about vitamin D deficiency. Infants and children under age 5 and pregnant and breastfeeding women are advised to take a daily supplement of vitamin D. However, national surveys indicate that update of vitamin D supplements is low, particularly among low income groups.

Healthy Start is a UK-wide, means tested, statutory scheme which aims to provide a nutritional safety net for low-income pregnant women, new mothers and for children under the age of 4 years, who are in receipt of qualifying income-related benefits or tax credits. Pregnant women under the age of 18 are also eligible for the scheme, regardless of whether or not they receive benefits. Healthy Start children's vitamins contain the recommended amount by UK health departments of vitamin A, C and D for children aged six months to four years and women's vitamins contain the recommended amount of folic acid, vitamin C and vitamin D for pregnant and breastfeeding women.

Uptake of Healthy Start vitamins is very low. Key barriers to uptake include practical difficulties with obtaining supplies of the vitamins, their short shelf-life, the complex ordering and reimbursement system, complicated assessment of eligibility and difficulties in identifying a convenient and accessible location through which they could be distributed. Making the scheme universally available may overcome some of these issues. The National Institute of Health and Care Excellence (NICE) recently released guidance in the implementation of existing guidance to prevent vitamin D deficiency which focuses on increasing uptake (1). NICE has commissioned research to investigate the differential cost-effectiveness between offering the scheme on the current targeted, versus a universal, basis. This cost-effectiveness review will inform the development of that research.

2. OBJECTIVES

The review considered the following research question:

- What evidence of cost-effectiveness of the vitamins contained within the Healthy Start supplement is available and does this evidence show supplementation to be cost-effective?

3. METHODS

All methods employed in this review were developed in accordance with the NICE public health methods manual (2) and through discussions with the NICE team and an expert reference group (ERG). In addition to database searches, citation searches were carried out, reference lists of all studies reviewed at full paper stage were reviewed and a call for any unpublished evidence was made to Healthy Start leads. Publications were selected based on criteria outlined in a review protocol developed with the research team, NICE team and the ERG. To be included in the review, studies had to investigate one of the eligible population groups (women planning a pregnancy, pregnant women, pregnant women with a child aged up to 12 months and infants or children aged up to five years). Eligible studies investigated one or more of the vitamins contained within the Healthy Start scheme, featured a comparator and reported economic outcomes. All selected papers were assessed for applicability and quality and relevant data were extracted. Narrative summaries and evidence statements were constructed taking into account the quality of findings and applicability to the research question.

4. FINDINGS

Nine studies met the inclusion criteria for the review and underwent quality appraisal (19, 31-38). Seven of the nine included studies were conducted in the UK (30, 32-38). All studies were completed after 2002. Two of the studies identified were formal economic evaluations, one was a cost-effectiveness analysis (CEA) (19) and one was a cost consequence analysis (CCA) (32). Two studies study investigated supplementation with folic acid (19, 31), seven investigated supplementation with vitamin D (30, 32-38) and no studies investigated supplementation with vitamin A or vitamin C. One study included women planning a pregnancy (19), eight studies included pregnant women (19, 31-34, 36-38), and six studies included women with a child up to 12 months (32-34, 36-38) and seven studies included children up to the age of 5 years (32-38).

Overall, the quality of the studies was poor. Seven were appraised as having very serious limitations (31, 33-38), one as having potentially serious limitations (19) and one as having minor limitations (32). Studies that were judged to be of poor quality had significant reporting omissions that meant it was not possible to have confidence in their reliability. Often this was because the studies were not intended to be formal economic evaluations. Because the studies were not intended to be formal economic evaluations it is unsurprising that they score poorly on the economic evaluations quality appraisal checklist. All of the studies were appraised as being partially applicable to the research questions. Two of the studies were submitted in confidence as a result of a call for evidence to Healthy Start leads and any information relating to these is highlighted in yellow.

Evidence statement one – vitamin A

In the population groups of interest there was no evidence identified that investigated the cost-effectiveness of vitamin A supplementation.

Evidence statement two – vitamin C

In the population groups of interest there was no evidence identified that investigated the cost-effectiveness of vitamin C supplementation.

Evidence statement three – vitamin D

There is weak evidence from six [very serious limitations] cost studies and moderate evidence from one [minor limitations] economic evaluation (CEA) about the costs of providing supplementation with vitamin D. The studies rated with 'very serious limitations' were not formal economic evaluations.

Only one study[1] carried out extensive sensitivity analysis, though all studies included some scenario analysis. All of the studies included treatment costs associated with vitamin D only. Supplementation was often costed with Healthy Start supplements in mind; however, relevant cost savings associated with all the vitamins provided by Healthy Start supplements were not included. Only one study was a formal economic evaluation and many studies included crude estimates of costs.

The results of the studies are inconclusive. Of the seven studies identified, three found vitamin D supplementation to be cost saving and four found it to be cost incurring

One study with moderate evidence[1] estimated that providing free supplements to the whole population of England and Wales resulted in an incremental cost of £4,086,142. The cost per symptomatic vitamin D deficiency averted was £2,859 for pregnant and breastfeeding women. The cost per symptomatic deficiency averted for children under 5 years was £1,229

One study[2] estimated that the costs of providing free supplementation in Greater Manchester Primary Care Trust (PCT) to all pregnant women, breastfeeding women for one year postnatally and children up to 5 years (£2,336,475) is less than the cost of treating vitamin D deficiency (£4,248,322) even when 100% uptake is assumed. In scenarios with a lower uptake, the cost of supplementing would be less. Another study[3] estimated that the cost of supplying free vitamin supplements to 25% or less of the citywide population of pregnant women and up to 12 months postnatally and children under four years in Birmingham PCT (£164,988) is less than treating vitamin D deficiency (£165,000). However, with 100% uptake the cost of supplying vitamin D is estimated to be £659,952. A study by Lambeth CCG[4] found that the costs of supplying vitamins to pregnant women, breastfeeding mothers one year postnatally and children up to 4 years in Lambeth and Southwark (year 1 = £180,342, year 2 = £118,195) is less than the cost of treating vitamin D deficiency (£383,102). A study in Greater Manchester[5] estimated that the net cost (cost of intervention minus reduction in treatment costs) of supplying pregnant women and 12 months postnatally and children under four years would be £152,920, that is, no overall cost saving. A further study in the same setting and population groups in Salford[6] estimated the net costs to be £73,932 (year 1), £37,063 (year 2) and £29,632, this diminishes over time but still indicates no overall cost saving. A further study[7] which included the costs of treating vitamin D deficiency and the costs of supplying vitamins found that the costs of supplementing children under 5 years in Burnley Health Care Trust compared to no free supplements being provided resulted in an incremental cost of supplying vitamin D according to COMA guidelines (supplementation for the first two years)* of £71,543 or £195,143 according to DH guidelines (supplementation for the first five years) at the time. It should be noted that the figures in the studies reported above are not comparable with each other due to the different population sizes in each study.

1 Filby *et al.,* 2014**
2 Turner *et al.,* 2012
3 McGee 2010
4 NHS Lambeth CCG, 2014
5 Salford CCG, 2013
6 Salford CCG, 2014
7 Zipitis *et al.,* 2006

* The reports refers to the following COMA report: Department of Health. Department of Health Report on Health and Social Subjects. 49 Nutrition and bone health with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food Policy. London: HMSO, 1998.

** In cases where reviewers were authors of an included study, data extraction and quality appraisal was undertaken by a reviewer completely independent to the study.

Evidence statement four – folic acid

In the population groups of interest there is moderate evidence from one study[1,] and weak evidence from one study[2]. One[1] [potentially serious limitations, partially applicable] economic evaluation on the cost-effectiveness of providing periconceptional supplementation of folic acid, compared to no folic acid supplementation in women planning a pregnancy and pregnant women and one[2] [very serious limitations, partially applicable] cost analysis of providing supplementation with multivitamins containined folic acid to pregnant women.

One study was carried out in a health-care setting in the Netherlands[1]. The study was appraised as having potential serious limitation mainly due to the lack of information reported. The authors did not fully report the model structure, resource use and units costs separately, cost sources and total cost, benefits were not reported separately and details about sensitivity analysis. The results showed that the incremental cost per discounted life-year gained through folic acid supplementation was £1,488.90. Univariate, multivariate and probabilistic sensitivity analyses were carried out. In the worst case scenario the cost per life year gained increased to £5,688.35; in the best case scenario the intervention was cost saving.

The second study was carried out in the US healthcare setting. The study was appraised as having very serious limitations as it was a cost analysis only and did not include health outcomes or any sensitivity analyses. The authors did not include all relevant costs. Providing supplementation with multivitamins containing folic acid to all pregnant women would cost £104 million and reducing the risk of NTDs and other conditions could prevent hospital charges of more the £832 million per year*.

1 Postma *et al.,* 2002
2 Bendich *et al.,* 1997
* Please note that although this study included other conditions (low birth weight and cardiovascular birth defects) in the economic evaluation, these are not outcomes of interest as defined in the scope for this project.

5. CONCLUSIONS

There is a sparse evidence base investigating the cost-effectiveness of providing supplementation in the specified population groups with the vitamins contained within the Healthy Start supplements.

Two studies investigated the cost-effectiveness of folic acid supplementation. The majority of the evidence identified investigated vitamin D supplementation in pregnant women, women in the first year postnatally and children up to the age of four or five years and the results from these studies were inconclusive. Of the seven studies identified, three found vitamin D supplementation to be cost saving and four found it to be cost incurring. Six of the seven studies were quality appraised as having very serious limitations. It is not possible to draw definitive conclusions about whether vitamin D supplementation in the population groups under consideration is, or is not, cost-effective based on these studies.

The results of this review suggest that further research is required into the cost-effectiveness of supplementation for women planning a pregnancy, pregnant women, women 12 months postnatally and children under 5 with the vitamins contained within the Healthy Start vitamin supplements.

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Abbreviations

BEN	Birmingham East and North Primary Care Trust
CCA	Cost consequence analysis
CCG	Clinical Commissioning Group
CEA	Cost-effectiveness analysis
CMO	Chief Medical Officer
COMA	Committee on Medical Aspects of Food Policy
CPH	Centre for Public Health
DH	Department of Health
ERG	Expert Reference Group
FSA	Food Standards Agency
GP	General Practitioner
ICER	Incremental cost-effectiveness ratio
LIDNS	Low Income Diet and Nutrition Survey
LRNI	Lower Reference Nutrient Intake
NDNS	National Diet and Nutrition Survey
NHS	National Health Service
NICE	National Institute of Health and Care Excellence
OECD	Organisation for Economic Cooperation and Development
PCT	Primary Care Trust
QALY	Quality-adjusted life year
QOL	Quality of life
YHEC	York Health Economics Consortium

Section 1: Introduction

The National Institute for Health and Care Excellence (NICE) Centre for Public Health (CPH) has commissioned York Health Economics Consortium (YHEC) to carry out a systematic cost-effectiveness review and an economic model. The purpose of this exercise is not to determine whether supplementation with Healthy Start vitamins as currently offered, is cost-effective but to estimate the differential cost-effectiveness between offering the scheme on the current targeted, versus a universal, basis.

1.1 BACKGROUND

In 2012, the Annual Report of the Chief Medical Officer (CMO) (3) ("Our children deserve better – Prevention pays") highlighted the importance of vitamin supplementation in mothers and young children and the growing concerns about vitamin D deficiency. The report argues that early prevention is key, but raises the question of how this is best implemented, highlighting a need for further research in this area.

> 'The growing concern over the prevalence of disease related to Vitamin D deficiency suggests to me that we should re-examine whether the Healthy Start vitamin programme should become a universal offering. There is a growing body of evidence to suggest that providing free vitamins to targeted groups has not led to high enough levels of uptake. This in turn has therefore not impacted on reducing the morbidity associated with vitamin deficiency. I am therefore recommending that NICE examines the cost effectiveness of the Healthy Start vitamin programme becoming universal' (Annual Report of the Chief Medical Officer, 2012, Chapter 1, pg. 5).

Healthy Start is a UK-wide, means tested, statutory scheme which aims to provide a nutritional safety net for low-income pregnant women, new mothers and for children under the age of 4 years, who are in receipt of qualifying income-related benefits or tax credits. Pregnant women under the age of 18 are also eligible for the scheme, regardless of whether or not they receive benefits (4). NICE's Maternal and child nutrition guidance (PH11) recommends providing Healthy Start vitamin supplements for eligible women (5).

Healthy Start beneficiaries receive vouchers that can be spent on milk, fruit and vegetables and formula. They also receive vitamin coupons for women's tablets or children's vitamin drops (4). The current project and protocol focuses only on the vitamin component of the Healthy Start scheme.

Healthy Start children's vitamins contain the recommended amount of vitamin A, C and D for children aged six months to four years and women's vitamins contain the recommended amount of folic acid, vitamin C and vitamin D for pregnant and breastfeeding women.

Vitamin C (ascorbic acid) is a water soluble vitamin with antioxidant properties, which is involved in wound healing and can enhance non-haem iron absorption and may, therefore, have a role to play in maintaining iron status. It has been suggested that that suboptimal status may play in role in chronic disease aetiology; however, evidence is contradictory (6). Chronic and severe vitamin C deficiency results in scurvy which is characterised by haemorrhages and abnormal bone and dentine formation, though this is very rare in the UK. With treatment full recovery from scurvy is expected (7, 8). Vitamin C was added to the Healthy Start supplements as a 'safety net'. The most recent results from the National Diet and Nutrition Survey Rolling Programme show that only 3.1% women have plasma vitamin C levels below that which indicates biochemical depletion (9). However, the Low Income Diet and Nutrition Survey (LIDNS) (10), which focuses specifically on low income households and which was carried out by the Food Standards Agency (FSA) from 2003-05, found that 16% of women aged 19 years and over had plasma vitamin C levels below 11µmol/l (indicating biochemical deficiency) and an additional 19% had levels between 11 and 28µmol/l (indicating biochemical depletion) (11). This illustrates the marked social gradient in vitamin C intakes.

Vitamin D is a general term to describe the group of steroid hormones that promote absorption of calcium and phosphorus in the intestine and regulate bone mineralisation. Severe vitamin D deficiency can result in rickets (among children) and osteomalacia (among children and adults). Vitamin D is essential for skeletal growth and bone health, but dietary sources in the UK are very limited. The major natural source of vitamin D is from skin synthesis following exposure to sunlight. From mid-October to the beginning of April in the UK, the population relies on stores accumulated in the summer, along with dietary sources of vitamin D.

The function of vitamin D during pregnancy remains unclear (12, 13). During pregnancy, poor maternal vitamin D status may adversely affect accumulation of infant vitamin D stores for their early months of life. Infants, who are exclusively breastfed, in particular for more than 6 months, are at increased risk as the amount of vitamin D in breast milk will not meet their needs. Infant formula sold in the UK is fortified with vitamin D but formula-fed infants with an intake of less than 500ml/day may not meet their vitamin D needs (14). Women of South Asian, African, Caribbean and Middle Eastern descent, and those who remain covered when outside, are at a particular risk of low vitamin D status, though some white women living at the most southerly latitudes of the United Kingdom have also been shown to be at risk (15).

For these reasons, the Scientific Advisory Committee on Nutrition recommend[1] that all pregnant and breastfeeding women, breastfed babies from the age of 6 months (or earlier if the mother's vitamin D status in pregnancy was not adequate), formula-fed babies receiving less than 500 ml formula a day and all children aged 1–4 years should receive vitamin D supplements (14). More recently, it has been recommended that all children aged from 6 months to 5 years take a supplement of vitamin D (3).

[1] The Scientific Advisory Committee on Nutrition is currently reviewing the dietary reference values (DRVs) for vitamin D. https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition#vitamin-d-working-group

However, despite initiatives such as the Healthy Start supplements, the Infant Feeding Survey (16) indicated that only 14% babies aged 8-10 months were given vitamin drops, though rates were markedly higher among babies from black and minority ethnic groups than among white babies (16). A booster sample of Healthy Start recipients in the Diet and Nutrition Survey of Infant and Young Children, indicated that only 6-7% of children aged 4-18 months were given vitamin supplements, either from Healthy Start or other sources (17).

While women planning a pregnancy and those in the first twelve weeks of pregnancy should be encouraged to increase their intake of dietary sources of folate and foods fortified with folic acid, these sources alone are insufficient to meet the recommended intake of 400 micrograms/day, for the prevention of neural tube defects (NTDs) such as spina bifida, anencephaly and encephalocele (18).

Neural tube defects are serious conditions and are the second most common group of birth defects. Anencephaly is fatal, resulting in stillbirth or in death shortly after birth. Children born with spina bifida have a high probability of being born with physical and mental disabilities (19). The direct medical costs and the indirect costs for the lifelong care of those born with spina bifida have been estimated to be significant (20) and it has been estimated that peri-conceptual supplementation with folic acid for the prevention of neural tube defects is cost-effective (19) (20).

When the recommendations about folic acid were first introduced, surveys showed that, while intial uptake of this folic acid was relatively high among some groups, it was lower among those on lower incomes and younger women. This applied particularly to the pre-conception period, where there was a marked disparity in uptake of the advice by socio-economic group and between women aged over, and under 25 years (21). More recently, the CMO's 2012 report (3) has highlighted a study of almost half a million women attending a London clinic between 1999 and 2012. This showed that while 35% of women planning a pregnancy between 1999 and 2001 were taking folic acid supplements , only 30% were doing so between 2011 and 2012. In addition, uptake was lower among younger women and those from some ethnic minority groups (22). Furthermore, it should be noted that around 50% of pregnancies are unplanned, and the women least likely to take folic acid supplements are those most likely to have unplanned pregnancies (23).

Timeliness of acting upon folic acid advice is a key issue. While the Infant Feeding Survey (16) reported that 79% mothers took folic acid in the first three months of pregnancy as recommended, only 37% took it pre-conceptually as also recommended, with 23% taking it later in pregnancy (16). Although folic acid is included in the Healthy Start vitamin supplement, concerns have been raised (24, 25) that women must be at least 10 weeks pregnant to be eligible for the scheme, and the time taken to register for the scheme may mean that the window of opportunity for folic acid supplementation has passed by the time women can access the vitamin supplements. This is particularly the case for first time pregnancies, where women are not already engaged with the scheme.

Vitamin A is needed for the normal functioning of the visual system, the maintenance of cell function, immunity and reproduction. While the National Diet and Nutrition Survey (NDNS) found that 6% of 1.5 to 3 year olds had intakes below the lower reference nutrient intake (LRNI), there were no children of this age range with plasma retinol levels associated with mild or severe deficiency. As with vitamin C, however, intakes vary across population sub-groups.

Vitamin A deficiency is extremely rare in the indigenous UK population. However, it is a major public health concern in developing countries and Public Health England has noted that practitioners should be alert to the possibility of vitamin A deficiency in at-risk migrant populations (PHE Online). It should be noted that vitamin A was originally added to Healthy Start supplements for children and vitamin C to the supplements for women as a nutritional safety net, for those most likely to have low intakes and to be nutritionally vulnerable (23).

Around 77% of those eligible for Healthy Start redeem their food vouchers. However, uptake of the vitamin supplements is low with two studies suggesting that uptake was less than 10% of those eligible (25, 26) and another suggesting that uptake was less than 3% (27). While this may be due in part to individual behaviour, other factors identified as contributing to low uptake include practical difficulties with obtaining supplies of the vitamins, their short shelf-life, the complex ordering and reimbursement system, complicated assessment of eligibility and difficulties in identifying a convenient and accessible location through which they could be distributed (24). Making the scheme universally available may overcome some of these issues. NICE has commissioned research to to estimate the differential cost-effectiveness between offering the scheme on the current targeted, versus a universal, basis. This cost-effectiveness review will inform the development of that research.

1.2 AIM AND RESEARCH QUESTIONS

The overarching aim of this work is to examine the cost-effectiveness of moving the Healthy Start vitamin programme from the current targeted offering, to a universal offering. The overall purpose of this exercise is not to determine whether supplementation with Healthy Start vitamins as currently offered, is cost-effective but to estimate the differential cost-effectiveness between offering the scheme on the current targeted, versus a universal, basis.

Two universal scenarios will be examined where the vitamins are offered to:

a) All pregnant women (from 10 weeks); women with a child aged under 12 months; and children over 6 months and under 4 years (as now). But regardless of their income level or their entitlement to the current qualifying benefits and tax credits;

b) All women planning a pregnancy; pregnant women; women with a child aged under 12 months; infants aged from 0 to 6 months; and children aged from 6 months to 5

years. (This is to reflect the UK dietary recommendations for folic acid supplementation and the CMO's 2012 recommendations for vitamin D)[2].

Primary research questions:

"Would it be cost-effective to move the Healthy Start Vitamin Programme from the current targeted offering to a universal offering, according to the following two scenarios?

a. Within the current parameters of the scheme (all pregnant women from 10 weeks; women with a child under 12 months; and children over 6 months and under 4 years;

b. All women planning a pregnancy; pregnant women; women with a child aged under 12 months; infants aged from 0 to 6 months and children aged from 6 months to 5 years."

Subsidiary questions are as follows:

1. "Is universal provision of Healthy Start supplements to women seeking to become pregnant cost-effective, compared with no provision under Healthy Start?"

2. "Is universal provision of Healthy Start supplements to women who are less than 10 weeks pregnant cost-effective, compared with no provision under Healthy Start?"

3. "Is universal provision of Healthy Start supplements for infants aged 0 to 6 months cost-effective, compared with no provision under Healthy Start?"

4. "Is universal provision of Healthy Start supplements for children aged 4 to 5 years cost-effective, compared with no provision under Healthy Start?"

5. "Would universal provision of supplements create a 'spill over' effect by increasing uptake in the current target group and would this be cost-effective compared with the current targeted offering?"

6. "What is the incremental cost-effectiveness ratio of extending the eligibility for universally available vitamins to:

- Infants from birth to 6 months compared with providing them for those aged over 6 months;
- Children between their fourth and fifth birthday compared with providing them until their fourth birthday;
- Women less than 10 weeks pregnant compared with providing them to those over 10 weeks pregnant (the current target);
- Women intending to become pregnant?"

[2] Infants aged 0-6 months are included in this scenario to reflect the UK dietary recommendations for vitamin D supplementation of breastfed babies whose mothers have not taken vitamin D supplements during pregnancy. It is also recommended that formula fed infants who may be receiving less than 500ml/day infant formula are given vitamin D supplements.

1.3 OBJECTIVES

The objective of the cost-effectiveness review is to inform this work by:

> Carrying out a systematic review of the evidence of the cost-effectiveness of supplementation with the vitamins contained within the Healthy Start vitamin programme.

The research question for the cost-effectiveness review is:

> What evidence of cost-effectiveness of the vitamins contained within the Healthy Start supplement is available and does this evidence show supplementation to be cost-effective?

1.4 IDENTIFICATION OF POSSIBLE EQUALITY AND EQUITY ISSUES

This cost-effectiveness review focuses on the following population groups:

- Women planning a pregnancy;
- Pregnant women;
- Women with a child up to 12 months old;
- Infants and children aged up to 5 years.

Therefore, there has been an inevitable emphasis on reviewing studies that included one or more of these population groups.

Section 2: Methodology

This cost-effectiveness review was conducted in accordance with the NICE public health methods manual (2). The review was guided by the NICE scope (28) which provides the rationale for the project, the overarching research questions and the relevant population groups. The review protocol was developed in close collaboration with both the NICE project team and an expert reference group (ERG).

2.1 INCLUSION AND EXCLUSION CRITERIA

The following selection criteria were applied to the search results.

2.1.1 Populations

To be included in this review, studies needed to investigate at least one of the sub-groups listed below:

- Women planning a pregnancy;
- Pregnant women;
- Women with a child up to the age of 12 months;
- Infants and children aged up to 5 years.

2.1.2 Interventions

Eligible studies were those that included interventions that aimed to provide vitamin supplementation with any of the following:

- Vitamin A (applies to children only);
- Vitamin C;
- Vitamin D;
- Folic acid (applies to women only);
- Any combination of the above including each vitamin alone;
- Multivitamins that comprised one or more of the vitamins above.

Studies that aimed to increase vitamin levels by any method other than with vitamin supplements, (for example, through diet, through exposure to sunlight, fortification or food supplements such as fish oils) were excluded. Studies in which the vitamin dose was more than double the Healthy Start vitamin dose were also excluded (there were no minimum dosage criteria applied for inclusion).

Although some studies may have contained minerals that interact with the vitamins specified above, (for example, vitamin D and calcium or vitamin C and iron) these were included in the searches and in the study selection. These studies were included due to the potentially small evidence base in this area and the possibility that the studies could contain key information. This approach was taken so that use of the best available evidence could be made.

2.1.3 Comparators

To be included in the review, a requirement was that studies must feature a comparator. The eligible comparators are:

- Any other eligible intervention (including the same vitamin distributed in a different way e.g. targeted vs universal provision);
- No activity.

2.1.4 Outcomes

Studies that reported one or more of the following outcomes were included:

- Cost per quality-adjusted life year (QALY);
- Cost per case of relevant condition/disease averted;
- Cost per life year gained;
- Cost per unit of benefit;
- Costs and benefits of an intervention presented as a cost-consequences analysis;
- Return on investment.

2.1.5 Study Features

Studies that were included in the review had the following study features:

- Published in 2000 or later;
- Published in English (as per NICE public health methods manual (2);
- Conducted within an Organisation for Economic Cooperation and Development (OECD) country.

2.1.6 Study Design

Studies which used any of the following designs were included:

- Cost-utility analyses;
- Cost-effectiveness analyses;
- Cost-benefit analyses;
- Cost-minimisation analyses;
- Cost-consequences analyses;
- Other study types that include economic data expected in the study designs outlined above.

Burden of disease and cost of illness studies were not be eligible for inclusion in the cost-effectiveness review.

2.2 METHODS OF STUDY IDENTIFICATION

Search strategies were designed and run to capture both published and unpublished evidence relevant to the review questions.

2.2.1 Bibliographic Database Strategies

Due to the relatively short timelines for the completion of the review, the search strategy adopted a reasonably pragmatic approach in order to maintain an acceptable level of precision. The strategy comprised three concepts; the intervention, the population, and study design. The strategy additionally searched for all material containing the phrase "Healthy Start" in the title or abstract of database records; this section of the strategy was not limited by population or study design to increase sensitivity and retrieve any relevant material missed by the three concept approach.

A sensitive search filter to identify economic evidence, adapted from the filter developed by the Centre for Reviews and Dissemination to retrieve records for the NHS EED database, was employed to retrieve the eligible study designs[3].

The intervention concept contained search terms (both keywords and subject headings) relating to the specific vitamins included in the Healthy Start supplements (folic acid and vitamins A, C and D), brand names of supplements aimed at the populations of interest and multivitamins/vitamin supplements generally. Studies on supplementation with a multivitamin were assessed at record screening stage to ensure that the intervention contains at least one of the vitamins contained in Healthy Start supplements.

[3] CRD Database Search Strategies http://www.crd.york.ac.uk/crdweb/searchstrategies.asp Accessed 24/06/14.

The strategy, where allowed by the database interface, removed non-English language publications, safely removed any animal studies and excluded any publication types that are unlikely to be relevant (case reports, news, editorial, letters and commentary). The search strategy was limited to studies published from 2000 to current.

Full search strategies are provided in Appendix B.

2.2.2 Electronic Databases and Websites

The following databases were searched via the specified interfaces:

- AMED (Allied and Complementary Medicine) (Ovid SP);
- ASSIA (Applied Social Science Index and Abstracts);
- CENTRAL (Cochrane Central Register of Controlled Trials) (Cochrane Library, Wiley);
- CINAHL (Cumulative Index of Nursing and Allied Health Literature) (EBSCONet);
- Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library, Wiley);
- Cochrane Database of Systematic Reviews (Cochrane Library, Wiley);
- Cost Effectiveness Analysis Registry (www.research.tufts-nemc.org/cear4/);
- Database of Abstracts of Reviews of Effectiveness (DARE) (Cochrane Library, Wiley);
- EconLit (Ovid SP);
- Embase (Ovid SP);
- HEED (Health Economic Evaluation Database) (EBSCO);
- Health Management Information Consortium (HMIC) (Ovid SP);
- Health Technology Assessment Database (HTA Database) (Cochrane Library, Wiley);
- MEDLINE and MEDLINE in Process (Ovid SP);
- NHS Economic Evaluation Database (NHS EED) (Cochrane Library, Wiley);
- Social Policy and Practice (Ovid SP).

The following resources to locate unpublished studies and other grey literature were also searched:

- NICE Evidence (https://www.evidence.nhs.uk/);
- NICE webpages (http://www.nice.org.uk/);
- Public Health Observatories webpages (http://www.apho.org.uk/);
- EPPI Centre databases (https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=185):
    - DoPHER;
    - TRoPHI.

To identify reports from individual health authorities that have carried out their own evaluations of Healthy Start, we undertook searches of Google using the site limit to restrict to the NHS or gov.uk domains. We additionally contacted two relevant mailing lists (the Expert Reference Group and the Healthy Start Leads contact list provided by the NHS Business Services Authority on behalf of the DH to NICE) via email in order to attempt to obtain any grey literature not identified elsewhere. Full text of the request for evidence email can be found in Appendix B.

Reference lists of any relevant systematic reviews published in the last five years that were identified by the searches, and the reference lists of studies assessed at full text record selection were checked by the reviewers for any additional evidence missed by other search methods. Citation searches were also conducted on the Healthy Start literature and studies assessed at full text using Science Citation Index, Social Science Citation Index and Google Scholar.

2.2.3 Running the Search Strategies and Downloading Results

Appropriate searches were conducted on each of the databases or resources listed in Section 2.2.2. The search strategies and results by resource are set out in Appendix B.

The search results were then downloaded into EndNote bibliographic software where they were de-duplicated using several algorithms.

2.2.4 Additional results

Following the ERG meeting on the 10 December 2014 it was agreed that included studies from a cost-effectiveness review carried out for NICE Public Health maternal child and nutrition guidance (29) should be also be considered as the ERG highlighted that many studies looking at the cost-effectiveness of folic acid would have been conducted in the 1990s. This was to enable search results showing the cost-effectiveness of folic acid supplementation pre-2000 to be considered. The maternal child and nutrition review (published in 2006) identified studies published from 1990. Seven studies were included in the maternal child and nutrition folic acid review. Four of these studies were published post-2000 and had already been identified in the previous Healthy Start searches. This resulted in three additional studies being included in the search results.

2.3 STUDY SELECTION

The search results were assessed and categorised according to the inclusion and exclusion criteria set out in Section 2.1. The numbers of records included and excluded at each stage of the study selection process were recorded and are presented in Section 3.1.

Two reviewers independently selected records by firstly screening the title and/or the abstract of the record. The full text documents of the studies thought to be relevant to the review were obtained. Studies that were excluded at the full paper screening stage have been tabulated along with their reason for exclusion, in Appendix C. To ensure a high degree of inter-rater reliability, the reviewers worked through a sample of studies meeting the inclusion criteria and discussed any relevance issues before both reviewers individually screening the rest of the retrieved studies.

2.4 QUALITY APPRAISAL, DATA EXTRACTION AND DATA SYNTHESIS

Each study was quality assessed using the economic evaluation checklist in Appendix I of the NICE public health methods manual (2). Two reviewers independently assessed the quality of the individual studies. Disagreements were resolved through consensus and if necessary a third reviewer was consulted. An assessment of applicability of the study to the current UK healthcare system and NICE decision-making was made, whereby studies were classified as:

- Directly applicable – the applicability criteria are met, or one or more criteria are not met but this is not likely to change the conclusions about cost-effectiveness;
- Partially applicable – one or more of the applicability criteria are not met, and this might possibly change the conclusions about cost-effectiveness;
- Not applicable – one or more of the applicability criteria are not met, and this is likely to change the conclusions about cost-effectiveness.

An assessment of the methodological quality of included studies was also undertaken, whereby studies had:

- Minor limitations – the study meets all quality criteria, or the study fails to meet one or more quality criteria, but this is unlikely to change the conclusions about cost-effectiveness;
- Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusion about cost-effectiveness;
- Very serious limitations – the study fails to meet one or more quality criteria and this is very likely to change the conclusions about cost-effectiveness.

One reviewer extracted the data from each of the included studies using a standardised template, and a second researcher checked the extraction. Any discrepancies were resolved through discussion or by consulting a third researcher. The data extraction tables can be found in Appendix D. The data extraction template for economic evaluation studies as presented in Appendix K3 of the NICE public health methods guide (2) was used. In cases where reviewers were authors of an included study, data extraction and quality appraisal was undertaken by a reviewer completely independent to the study.

Data synthesis incorporated narrative summaries and evidence tables for all studies and provided concise detail on: populations, intervention, settings and outcomes. Results were presented in the most appropriate format for each population group to reflect the number of studies identified, the quality of the studies, and the different types of studies included. Where a non-UK study was included, the results were converted into pounds sterling using the appropriate purchasing power parity (30). Where studies were submitted in confidence the relevant data have been highlighted in yellow.

EndNote reference management software and Microsoft Excel were used for the record selection and coding of studies. Word 2007 tables were used for the data extraction.

Section 3: Results

3.1 SEARCH RESULTS

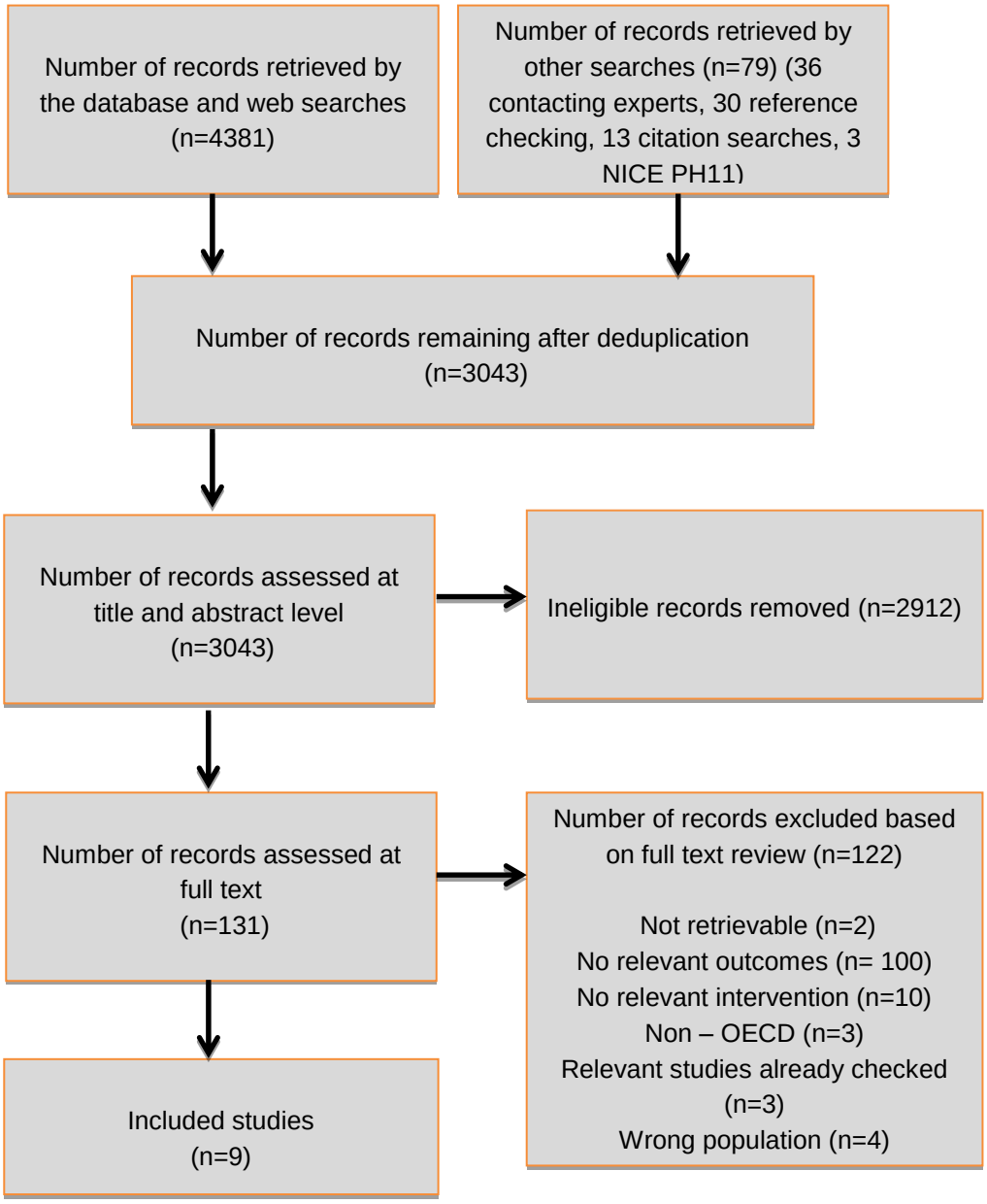
The searches identified 4,460 records, leaving 3,043 once duplicate records were removed. The source of these records can be found in the PRISMA diagram (Figure 3.1).

550 records were removed at screening stage by an experienced information specialist in EndNote. This screened out obviously irrelevant records, specifically studies which were:

- Animal or other non-human populations;
- Case reports;
- Non OECD settings;
- Non English language;
- Not a relevant intervention;
- Not a relevant population.

The remaining 2,493 records were passed to the reviewers for further assessment. Of these, 131 studies were identified as being potentially relevant to the review based on the title and abstract and the full paper of these was screened. Of the full papers screened, 9 studies met the inclusion criteria for the review.

Figure 3.1: PRISMA flow chart



3.2 OVERVIEW OF STUDIES SELECTED

Nine studies met the inclusion criteria and underwent quality appraisal (Appendix E). Seven studies were identified as having very serious limitations, one had potentially serious limitations and one had minor limitations (see Table 3.1). Those studies with 'very serious limitations' were not formal economic evaluations. Because the studies were not intended to be formal economic evaluations it is unsurprising that they score poorly on the economic evaluations quality appraisal checklist. Seven of the included studies were conducted in the UK. One study was carried out in the Netherlands (19) and one in the US (31). Two of the studies were submitted in confidence as a result of a call for evidence and any information relating to these is highlighted in yellow.

All of the studies included at least one of the population groups specified in Section 2.1.1. One study included women planning a pregnancy (two studies mentioned women planning a pregnancy in their potential population group but this was not included in the calculations), eight studies included pregnant women, six studies included women with a child up to the age of 12 months (or they included breastfeeding women) and seven studies included infants and children aged up to 5 years. Only one of the studies (32) reported results for separate population sub-groups, the remaining studies reported combined results for all the relevant populations.

Seven studies investigated supplementation with vitamin D, five of these studies supplemented with Healthy Start vitamins, however, the main focus was on vitamin D supplementation although two of these studies also (33, 34) included the cost avoidance of prescribing folic acid. Two studies investigated supplementation with folic acid and no studies were identified that investigated the cost-effectiveness of supplementation with vitamin A or C.

The studies are presented in Table 3.1 which provides an overview of the studies by population group and by which vitamin supplementation was provided.

Table 3.1: Studies that met the inclusion criteria by population group and vitamin

Study citation. Setting	Study design	Population group	Vitamin	Quality score / applicability
Zipitis *et al.,* 2006 (35). Burnley	Cost analysis	Children under 5 years	Vitamin D	Very serious limitations / Partially applicable
Turner *et al.,* 2012 (33). Manchester	Cost analysis	Pregnant women. Breastfeeding mothers (which will include those 12 month postnatally). Children up to the age of 5.	Healthy Start supplements (with particular regard to vitamin D)	Very serious limitations / Partially applicable
McGee, 2010 (36). Birmingham	Cost analysis	Pregnant women. Women 12 months postnatally. Children under 4 years.	Healthy Start supplements (with particular regard to vitamin D)	Very serious limitations / Partially applicable
Postma *et al.,* 2002 (19). Netherlands	Economic evaluation (CEA)	Women planning a pregnancy. Pregnant women.	Folic acid	Potentially serious limitations / Partially applicable
Filby *et al.,* 2014 (32). UK[4]	Economic evaluation (CCA)	Pregnant and breastfeeding women. Children under the age of 5 years.	Vitamin D	Minor limitations / Partially applicable
NHS Lambeth CCG, 2014 (37). UK	Cost analysis	Pregnant women. Breastfeeding mothers (up to the age of one year of the baby). Children up to the age of 4 years.	Healthy Start supplements (with particular regard to vitamin D)	Very serious limitations / Partially applicable
Salford CCG, 2013 (38). UK	Cost analysis	Pregnant women. 12 months postnatally. Children under 4 years.	Healthy Start supplements (with particular regard to vitamin D)	Very serious limitations / Partially applicable
Salford CCG, 2014 (34). UK	Cost analysis	Pregnant women. 12 months postnatally. Children under 4 years.	Healthy Start supplements (with particular regard to vitamin D)	Very serious limitations / Partially applicable
Bendich *et al.,* 1997 (31)	Cost analysis	Pregnant women	Multivitamin containing folic acid	Very serious limitations / Partially applicable

[4] In cases where reviewers were authors of an included study, data extraction and quality appraisal was undertaken by a reviewer completely independent to the study.

3.3 FINDINGS

3.3.1 Narrative Summary

Nine studies met the inclusion criteria. All studies were quality appraised as partially applicable. Three studies were full peer review publications, one [very serious limitations] was based in the UK (35), one [potentially serious limitations] was based in the Netherlands (19) and one [very serious limitations] was based in the US (31). One study [minor limitations] was a report for NICE to support guidance development (32). The remaining studies were local reports; all were quality appraised as having very serious limitations.

As stated above there were no studies identified investigating supplementation with vitamin A or with vitamin C. Two studies investigated folic acid and the remaining studies investigated supplementation with vitamin D. Table 3.2 contains a summary of each eligible study by population group. Full data extraction tables are available in Appendix D.

Table 3.2: Evidence table by population group

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
Women planning a pregnancy					
Postma *et al.,* 2002 (19) To estimate the cost-effectiveness of periconceptional supplementation of folic acid using pharmacoeconomic model calculation Economic evaluation (CEA) Quality score: Potentially serious limitations Applicability: Partially applicable	Women planning a pregnancy. Pregnant women. Health–care setting in the Netherlands (including indirect costs)	Intervention: Folic acid supplementation (0.5mg, daily) from at least 4 weeks before until at least 8 weeks after conception. Comparator: No folic acid supplementation (current pattern of care in the Dutch setting)	Costs and benefits (measured as life-years gained) of the interventions including supplementation and the cost of health outcomes.	The incremental cost per discounted life-year gained was £1,488.90	Data sources are generally not clearly described. The study was published in 2002 in the Netherlands and it may not be directly applicable to the current UK healthcare perspective.
Pregnant women					
Turner *et al.,* 2012 (33) The aim of this project was to investigate the potential health effects of universal access to Healthy Start vitamins with particular regard to Vitamin D in all pregnant women and breastfeeding mothers and children up to the age of 5 within Greater Manchester. Cost analysis Quality: Very serious limitations Applicability: Partially applicable	Pregnant women and breastfeeding mothers up to one year postnatally and children up to the age of 5. Greater Manchester.	Intervention**:** Universal supplementation of vitamin D (with Healthy Start vitamins) in target group Comparator: Vitamin supplementation as present No comparative analysis was conducted.	Cost of vitamin supplementation Cost of treating vitamin deficiency.	Cost of supplying universally assuming 100% uptake: £2,336,475. Cost after claiming back HS costs from Department of Health (DH): £1,676,592 Savings from reduced spending on treatment for vitamin D deficiency: £4,248,322 Other savings could sum to £6,260,322 (reduced spending on prescribing folic acid, treatment of rickets). Results showed cost-savings with universal supplementation.	Report includes some crude estimates of costs. All relevant costs not included. Sources for costs were not provided. Costs were reported over 3 years and no discounting was applied. The report focuses on vitamin D deficiency costs, no treatment relating to deficiency of the other vitamins supplied in HS are considered.

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
McGee, 2010 (36) To estimate the cost of universal vitamin D supplementation for pregnant women (and up until their child is 12 months old) and children up to four years old, in Birmingham Cost analysis Quality: Very serious limitations Applicability: Partially applicable	Pregnant women and until the infant is 12 months old. Also, children under 4 years old. Birmingham	Intervention: Universal vitamin D supplementation (with Healthy Start vitamins). Scenario 1: All pregnant women and postnatal women and children under the age of 4. Scenario 2: All pregnant and postnatal women and only those children covered under the Healthy Start scheme. Comparator: No universal supplementation	Cost of vitamin supplementation for target groups. Cost of treating vitamin D deficiency.	Annual cost of supplying vitamins in scenario 1: 100% uptake £659,952. 10% uptake in two Primary Care Trust's (PCTs) and 25% uptake in one PCT £102,984. 25% uptake for women and children citywide (all three PCTs) £164,988. Estimated cost of treated rickets for one year = £5,000 x 33 cases = £165,000. Annual cost of supplying vitamins in scenario 2: 100% uptake £124,414. 25% uptake £31,103. Results showed cost savings with 10% uptake.	Source of treatment cost was not reported. All relevant costs were not included. Only vitamin D related treatment costs were included. The Healthy Start vitamins include other nutrients which may offer other benefits which may not have been accounted for
Filby *et al.,* 2014 (32) (report for NICE)[4] The overall aim of this project was to provide an estimate to NICE of the cost-effectiveness of interventions to increase awareness of vitamin D guidance The economic evaluation assessed the economic impact of a campaign carried out in Birmingham to promote universal uptake of vitamin D supplementation among pregnant and breastfeeding women and children under the age of 5 years.	Pregnant and breastfeeding women. Children under the age of 5 years. NHS in England and Wales.	Intervention: Universal supplementation of vitamin D (cost of Healthy Start vitamins applied) Comparator: No universal supplementation of vitamin D	Number and cost of symptomatic vitamin D deficiency (cost of symptomatic vitamin D was taken from Zipitis (2006)) (35) and the total cost associated with the intervention implementation. The cost per	Total costs were £14,197,855 before the intervention and £18,463,596 after the intervention, resulting in an incremental cost of £4,256,741 for the whole eligible population. The cost per deficiency averted was £2,859 for pregnant/breastfeeding women. Results showed it was cost-incurring to promote universal	Uncertainty around the estimation of several inputs and use of assumptions.

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
Economic analysis (CCA). Quality score: Minor limitations Applicability: Partially applicable			deficiency averted was also reported.	supplementation.	
NHS Lambeth CCG, 2014 (37) To estimate the economic impact of universal supplementation of vitamin D for all mothers during pregnancy and until their child is 12 months old, and for all children under 4 years old in the area of Lambeth and Southwark (UK) Cost analysis Quality score: Very serious limitations Applicability: Partially applicable	Pregnant women. Breastfeeding mothers (up to the age of one year of the baby). Children up to the age of 4 years. Lambeth and Southwark.	Intervention: Universal supplementation of vitamin D (with Healthy Start vitamins) Comparator: Universal supplementation of vitamin D is solely for babies up to 6 months of age (current standard of care)	Costs to the health care payer considering the extra costs of universal provision of vitamin D minus the savings due to the reduced costs associated with lower incidence of vitamin D deficiency.	The expected costs of the intervention are £180,342 for the first year (£90,171 for Southwark and £90,171 for Lambeth) and £118,195 for subsequent years (£59,097.50 for each borough). The costs associated to vitamin D deficiency and rickets in Lambeth & Southwark which is estimated to cost £383,102 per annum (much higher than the cost of programme implementation). Results showed that it was cost-saving to implement universal supplementation.	Does not derive a comprehensive benefit measure of the health impact of the proposal. Only vitamin D related costs were included. The Healthy Start vitamins include other nutrients which may offer other benefits which may not have been accounted for.
Salford CCG, 2013 (38) To assess the economic impact of universal supply of vitamin D for targeted groups Cost analysis Quality score: Very serious limitations Applicability: Partially applicable	Pregnant women. 12 months postnatally. Children under 4 years Greater Manchester and Salford.	Intervention: Universal provision of vitamin D (with Healthy Start vitamins) Comparator: No universal supply of vitamin D	Costs of universal provision of vitamin D supplementation and the cost savings due to a reduction of resource use associated with treatment of vitamin D deficiency	The yearly costs of universal provision of vitamin D supplementation were £1,821,437 (£1,323,323 after reclaims from DH) in Greater Manchester and £182,144 (£132,332 after reclaims from DH in Salford). In the latter setting, namely Salford, assuming a 10% incidence reduction, the net cost of the intervention would be £121,140. If including the	Does not derive a comprehensive benefit measure of the health impact of the proposal. Only vitamin D related treatment costs were included. The Healthy Start vitamins include other nutrients which may offer other benefits which may not have been accounted for.

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
			consequences	distribution costs, the net cost would be £152,920. Results showed it was cost-incurring to introduce universal supplementation.	
Salford CCG 2014 (34) To estimate the economic impact of universal supplementation of Healthy Start vitamins for targeted groups in Salford, UK Quality score: Very serious limitations Applicability: Partially applicable	Pregnant women. 12 months postnatally. Children under 4 years. Salford.	Intervention: Universal supplementation of Healthy Start vitamins (focus on vitamin D). Comparator: The implicit comparator was the current pattern of care, which is the doing-nothing option	Costs to the health care payer considering the extra costs of universal supplementation of Healthy Start vitamins (running costs, costs of vitamins, and costs of publicity) minus the savings due to the financial (tangible) benefits (directly correlated to uptake)	The expected net costs of the service are £73,932 for year 1, £37,063 for year 2, and £39,632 for year 3. Results showed it was cost-incurring to introduce universal supplementation.	Focused mainly on the financial impact (extra costs and savings) of the intervention. No measure of benefit was estimated. Only vitamin D related health outcome treatment costs were included (rickets). The Healthy Start vitamins include other nutrients which may offer other benefits which may not have been accounted for.
Bendich et al., 1997 (31) To use published risk estimates associated with vitamin supplement intake to project potential annual cost reductions in US hospitalisation charges Quality score: Very serious limitations Applicability:	Pregnant women US	Intervention: Vitamin supplementation with multivitamins containing folic acid. Comparator: No supplementation is implied	The outcomes of the intervention were measured in terms of the costs to the health care system of NTDs considering the extra costs of providing	Based on retail prices, the cost of providing multivitamins with folic acid supplementation for pregnant women costs £104 million. The authors calculate that reducing the risk of NTDs and other conditions at the same time, could prevent hospital charges of more than £832 million per year, which is a cost saving.	No health outcomes were included. No sensitivity analyses were reported. No model structure was reported as this was as a cost analysis.

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
Partially applicable			vitamin supplementation minus the cost of avoidable hospital charges and the lifetime cost of NTDs.		
Postma *et al.,* 2002 (19)	As reported above	As reported above	As reported above	As reported above	As reported above
Women with a child up to the age of 12 months					
Turner *et al.,* 2012 (33)	As reported above	As reported above	As reported above	As reported above	As reported above
McGee, 2010 (36)	As reported above	As reported above	As reported above	As reported above	As reported above
Filby *et al.,* 2014 (32)[4]	Pregnant and breastfeeding women included this subgroup.	As reported above	As reported above	As reported above	As reported above
NHS Lambeth CCG, 2014 (37)	As reported above	As reported above	As reported above	As reported above	As reported above
Salford CCG, 2013 (38)	As reported above	As reported above	As reported above	As reported above	As reported above
Salford CCG, 2014 (34)	As reported above	As reported above	As reported above	As reported above	As reported above
Infants and children aged up to 5 years					
Turner *et al.,* 2012 (33)	As reported above	As reported above	As reported above	As reported above	As reported above
McGee, 2010 (36)	As reported above	As reported above	As reported above	As reported above	As reported above
Filby *et al.,* 2014 (32)[4]	As reported above	As reported above	As reported above	The cost per deficiency averted was £1,229 for children under 5 years.	As reported above
Zipitis *et al.,* 2006 (35). To verify whether vitamin D deficiency is re-emerging in the catchment area since funding of vitamin D supplementation by Primary Care	Vitamin D deficient paediatric patients presenting at a	Intervention: 1. Supplementation with vitamin D if DH recommendations at the time	Cost of treating vitamin D deficiency and the cost of primary	The total cost of treating one vitamin D deficiency was £2,505 per patient. The cost of preventing one	Study was retrospective. Generalisation of results is problematic. Small sample size. Not

Study details: author, year, aim, design, quality ratings	Population and setting	Intervention and comparators	Outcomes	Results	Limitations
Trusts ceased, and to assess the cost-effectiveness of reintroducing vitamin D supplementation in the Burnley Health Care NHS Trust. Cost analysis Applicability: Partially applicable Quality: Very serious limitations	hospital paediatric department in Burnley, UK. Supplementation to give provided to all children under 5 years.	(supplementation for the first 5 years) were implemented in Burnley NHS Trust. 2. Supplementation with vitamin D if COMA[5] guidelines at the time (supplementation for the first 2 years) were implemented in Burnley NHS Trust. Comparator: No free supplementation offered.	prevention.	case of vitamin D deficiency in the Trust's child population was £19,014 (COMA) or £47,535 (DH). Total annual cost of primary prevention for whole Trust population was £82,400 (COMA) or £206,000 (DH) Incremental costs of supplementation versus no supplementation were increased costs of £71,542.50 (COMA) or £195,143 (DH).	all the health effects of supplementation with Abidec (a multivitamin) were considered. Not all relevant costs were included.
NHS Lambeth CCG, 2014 (37)	As reported above	As reported above	As reported above	As reported above	As reported above
Salford CCG, 2013 (38)	As reported above	As reported above	As reported above	As reported above	As reported above
Salford CCG, 2014 (34)	As reported above	As reported above	As reported above	As reported above	As reported above

[5] The reports refers to the following COMA report: Department of Health. Department of Health Report on Health and Social Subjects. 49 Nutrition and bone health with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food Policy. London: HMSO, 1998. The DH recommendations refer to the following: Chief Medical Officer. Meeting the need for vitamin D. CMO Update 2005;42:6 (available at http://www.dh.gov.uk/assetRoot/04/11/56/64/ 04115664.pdf, accessed 28 July 2006)

Postma *et al.* conducted a cost-effectiveness analysis [potentially serious limitations] of periconceptual supplementation of folic acid compared to no folic acid supplementation in the Dutch health care setting. The aim was to estimate the cost-effectiveness of introducing periconceptual folic acid supplementation to women planning a pregnancy and pregnant women. The model took a societal perspective but only included direct costs and benefits (such as hospital admissions directly related to birth, and costs of residential care for those with a disability and adaptations to private homes and costs of special education). Indirect costs (such as those related to production losses through lost work time) were omitted from the analysis. The authors calculated the net costs which were the total costs of supplementation minus the benefits of those costs averted by reducing NTDs. The life years gained were calculated by comparing the life-years that were lost with and without folic acid supplementation. Cost-effectiveness was expressed in net costs per discounted life-year gained (19).

The results showed that periconceptional supplementation of folic acid was estimated to cost £1,489 per discounted life year gained in the base case analysis. The authors also carried out univariate sensitivity analysis on the effectiveness, folic acid costs and costs of care for spina bifida inputs. The authors also carried out multivariate and probabilistic sensitivity analysis. The sensitivity analyses results ranged from £534 to a maximum of £5,421. The results remained mostly below £3,818 (19).

The authors acknowledge that this analysis would have been strengthened by including the use of quality of life (QOL) in order to calculate quality-adjusted life years (QALYs). There were also some issues with the transferability of costs from a US source to apply within the Dutch health care system. There may be some issues transferring both of these sources to the UK health care system. The model used some assumptions where there were gaps in the data, however, those that were made tended to be conservative assumptions and therefore this economic evaluation may underestimate the benefits of providing periconceptional folic acid supplementation (19).

Bendich *et al.* carried out a cost-analysis [very serious limitations] of supplementation with multivitamins containing folic acid in the US healthcare setting. The aim was to use published risk estimates associated with vitamin intake to project potential annual cost reductions in US hospitalisation charges. The study searched for relative risk estimates for birth defects, premature birth and coronary heart disease with vitamin intake. Only the components of the work associated with folic acid supplementation are reported here. It is not clear what perspective the model takes, it appears to be the healthcare system with a societal lifetime cost of NTDs. The authors calculated that providing multivitamins with folic acid for all pregnant women would cost (£104 million. Reducing the risk of NTDs and other conditions at the same time could prevent hospital charges of more than £832 million per year[6].

This was a cost analysis and did not include any health outcomes. As it is a cost analysis there was no model structure reported. Further, there were no sensitivity analyses reported

[6] Please note that although this study included other conditions (low birth weight and cardiovascular birth defects) in the economic evaluation, these are not outcomes of interest as defined in the scope for this project.

and not all relevant costs were included. The study only included the cost of buying the vitamins, but there were no costs or discussion about how these were to be distributed. There may also be some issues transferring this analysis to the UK health care system.

Although not a formal economic evaluation, Zipitis *et al.,* [very serious limitations] addressed the cost-effectiveness of vitamin D supplementation in a UK setting within Burnley Health Care NHS Trust. The authors estimated that it would cost £2,505 to treat one case of vitamin D deficiency in a paediatric department (35).

The cost of providing vitamin D supplementation to the total child population was estimated to be £206,000 per year or £82,400 per year according to the DH guidelines or those proposed by the Committee on Medical Aspects of food and Nutritional Policy (COMA)[7], respectively. The guidelines referred to are those available at the time of the study. DH guidelines at the time recommended provideing vitamin D supplementation for the first 5 years while COMA guidelines at the time recommended providing supplementation for the first 2 years. Providing supplementation to the entire population was estimated to avoid 4.33 cases of vitamin D deficiency, saving £10,857 per year. Therefore, the incremental costs of supplementation versus no supplementation were £71,543 or £195,143 according to the COMA and DH guidelines, respectively. For the Trust's population where the incidence of vitamin D deficiency was 1 in 923, the additional costs to prevent one case of rickets were £19,014 (COMA guidelines) and £47,535 (DH guidelines) (35).

The study did not include any costs other than the costs of the vitamin supplements when estimating the total cost of primary prevention. The costs that were included were of Abidec (a multivitamin). The true prevalence of vitamin D deficiency in the local childhood population was not determined in this study. It was a retrospective study, and the authors acknowledged that the low socioeconomic status of the population studied may render generalisation of the results and recommendations problematic. The study also had a small sample size. It did not include health benefits and costs for the other vitamins contained in Abidec supplementation. The focus of this study concerned only vitamin D supplementation (35).

[7] The reports refers to the following COMA report: Department of Health. Department of Health Report on Health and Social Subjects. 49 Nutrition and bone health with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food Policy. London: HMSO, 1998. The DH recommendations refer to the following: Chief Medical Officer. Meeting the need for vitamin D. CMO Update 2005;42:6 (available at http://www.dh.gov.uk/assetRoot/04/11/56/64/ 04115664.pdf, accessed 28 July 2006)

As part of a rapid health impact assessment exercise, Turner *et al.,* conducted a cost analysis [very serious limitations] of providing free vitamin D supplementation to pregnant and breast feeding mothers up to one year postnatally, and children up to five years old, in the Greater Manchester area. Vitamin D supplementation in this study was supplied by giving Healthy Start supplements. The study reported estimates of possible cost savings as a result of reduced spending on treatment for vitamin D deficiency. It also reported 'other' savings which included reduced spending on prescribing folic acid and treatment of biochemical rickets. Costs were estimated based on number of live births in Greater Manchester. The total cost of providing supplementation with 100% uptake for everyone in the target group was estimated to be £2,336,475. Assuming that in the first year uptake was 10% among the target group the cost would be £233,648 (£167,659 if all Healthy Start vitamin coupons were claimed for). This estimate is simply 10% of the total cost of £2,336,475. In the second year if uptake was 16% costs would be £373,836 (£268,255 if all Healthy Start coupons were claimed for). In the third year, if uptake was 25% costs would be £584,119 (£419,148 if all Healthy Start coupons were claimed back). Possible cost savings included the costs of treating vitamin D deficiency in women and children (£4,248,322), and other savings including treatment of rickets (60 to 200 cases of biochemical rickets per year) and reduced spending on folic acid in pregnancy (£6,260,322) (33).

Due to the nature of the exercise, estimated costs were very approximate and sources were not provided for these costs. No other costs related to staff training or administration of the scheme were considered. The report focuses only on vitamin D deficiency, although it reports the costs saving on prescribing folic acid, no other health benefits or costs from the vitamins supplied by Healthy Start vitamin supplements are included (vitamin A, vitamin C, folic acid) (33). Further, the study took a local perspective and therefore did not include the costs of vitamins to the DH.

McGee carried out a study [very serious limitations] making the case for a roll out of universal vitamin D supplementation from one inner city Primary Care Trust (PCT) (HoB) to two additional Birmingham PCTs (Birmingham East and North PCT (BEN) and South Birmingham PCT). The aim was to make the scheme available to the target group (women who were pregnant or whose child was under 12 months old and children under four years old) using Healthy Start supplements to provide vitamin D supplementation. The report included estimates of the cost of providing free universal supplementation to the target groups in the three PCTs and compared them to the estimated costs of treating vitamin D deficiency in children in the same three PCTs. The costs of the intervention comprised the purchase cost of vitamins minus the cost of vitamins supplied to those eligible for Healthy Start, as well as charges for delivery to distribution points (36).

From the perspective of the PCT, the total cost of providing free universal vitamin D supplementation to the target groups with 100% uptake in the three PCTs was estimated at £659,952. The author considered this to be a huge over estimate of what a universal policy might cost as, after 4 years and much awareness-raising in HoB, only 18% of women and 11% of eligible children were receiving the vitamins. Assuming 10% uptake for both women and children in South and BEN PCTs, plus 25% uptake in HoB for the year 2011-12 the total cost was estimated to be £102,984. Assuming 25% uptake for both women and children citywide in subsequent years the total cost was estimated to be £164,988. A second scenario was also considered in which the universal supplementation was provided to all pregnant and postnatal women and only to those children covered under the Healthy Start scheme. In the second scenario, assuming full reclaims from the DH, 100% uptake would cost £124,414 and 25% uptake would cost £31,103. The study estimated the cost of treating one case of nutritional rickets to be £5,000 and, therefore, the cost of treating the 33 identified cases of rickets or hypocalcaemic fits in Birmingham in 2009- 2010 was estimated to be £165,000 (36).

It should be noted that this was not a formal economic evaluation. The approach taken in this study implicitly ignored any additional health benefits of vitamin D supplements other than preventing new cases of vitamin D deficiency in children. It did not include all relevant costs associated with the intervention and it did not cite the source of the estimated cost of treating vitamin D deficiency. It also did not include any benefits or costs associated with the other vitamins provided in the Healthy Start supplements (vitamin A, vitamin C and folic acid) (36). Further, the study took a local perspective and therefore did not include the costs of vitamins to the DH.

Filby *et al.,* conducted an economic evaluation (CCA) funded by NICE [minor limitations] which investigated providing vitamin D supplements targeted or universally. Filby *et al.* was developed by the some of the authors of this report. Where the current report authors were involved in the development of included studies, the included study was data extracted and quality appraised by someone independent of the project. The overall aim of this project was to provide an estimate to NICE of the cost-effectiveness of interventions to increase awareness of vitamin D guidance. The economic evaluation assessed the economic impact of a campaign carried out in Birmingham to promote universal uptake of vitamin D supplementation among pregnant and breastfeeding women and children under the age of 5 years. The model took an NHS England and Wales health care system perspective. A conventional cost-consequence analysis was carried out which included the costs of implementing the intervention, supplying the vitamins and treating symptomatic vitamin D. The outcome was the number of cases of symptomatic vitamin D averted (32).

The cost per deficiency averted for pregnant and breastfeeding women was £2,859 and for children under 5 years this was £1,299. The total costs for both population groups combined were £14,197,855 before the intervention and £18,463,596 after the intervention resulting in an incremental cost of £4,256,741. Sensitivity analyses showed that increasing the baseline prevalence of deficiency resulting in increased cost-savings. They also showed that, based on the inputs included in the model base case, the intervention was cost-saving for pregnant

and breastfeeding women up to an intervention cost of around £1.5 million, while for children, the intervention was never cost-saving (32).

The authors acknowledge that there was a great deal of uncertainty around the estimation of several of the model inputs. The analysis did not include QOL inputs and consequently QALYs were not calculated. If the data were available, QALYs would be a useful measure to calculate. This analysis only looked at costs and outcomes associated with supplementation of vitamin D, not the other vitamins included in Healthy Start supplements (32).

NHS Lambeth Clinical Commissioning Group (CCG) carried out a cost analysis [very serious limitations] with the aim of estimating the economic impact of universal supplementation for all mothers during pregnancy and until their child is 12 months old, and for all children under four years in the Lambeth and Southwark areas. The report includes the cost of distributing the vitamins which accounts for the costs of the vitamins, staff costs to co-ordinate the scheme including raising awareness and implementing the scheme in the first year; overheads for the staff member, training and supervision. Costs of the wholesale licensing fee was included (this is necessary to distribute vitamins via different centres and/or pharmacies). A cost to incentivise Healthy Living pharmacies to distribute the vitamins was also included. Finally, this proposal planned to utilise a vitamin card scheme, where the vitamin card is a means of registering and distributing the vitamins, a first year set up cost (£22,559) was given; this would be reduced to approximately £5,000 in following years. Potential costs averted included acute admissions, outpatient costs, testing costs and primary care prescribing costs (37).

The expected costs of the intervention are £180,342 for the first year (£90,171 for Southwark and £90,171 for Lambeth) and £118,195 for subsequent years (£59,098 for each borough). The costs associated with vitamin D deficiency and rickets in Lambeth & Southwark was estimated to cost £383,102 per annum (much higher than the cost of programme implementation) (37).

This was not a formal economic evaluation and focused on the budget impact of the intervention. Incremental costs were not calculated but can be derived from the figures provided in the paper. It also did not include any benefits or costs associated with the other vitamins provided in the Healthy Start supplements (vitamin A, vitamin C and folic acid) (37). Further, the study took a local perspective and therefore did not include the costs of vitamins to the DH.

Salford CCG (2013) carried out a cost analysis [very serious limitations] which aimed to assess the economic impact of the universal supply of vitamin D for pregnant women, breastfeeding women up to one year postpartum and infants and children up to the age of 4 years in Greater Manchester and Salford. The cost analysis utilised figures from a Rapid Health Assessment of the effect of vitamin D for women and children in Greater Manchester which was also included study in the review and is summarised above (33). The costs in this evaluation consisted of the cost of treatment for vitamin D deficiency (taken from the Rapid Health Assessment), the cost of vitamin supplements, the cost of vitamins after reclaim from the DH and an indicative cost of a central distribution hub (cost of staff, storage,

premises, consumables and carriage). The report mentioned the need to carry out engagement exercises, a training programmes and a media campaign. However, these costs were not included in the evaluation (38).

The yearly costs of universal provision of vitamin D supplementation, including distribution cost were £1,821,437 (£1,323,323 after reclaims from DH) in Greater Manchester and £182,144 (£132,332 after reclaims from DH) in Salford. In the latter setting, namely Salford, assuming a 10% incidence reduction per year, the net cost of the intervention would be £152,920, with 16% reduction the net cost would be £146,204 and with a 25% reduction the net cost would be £136,131 (38).

This was not a formal economic evaluation and focused on the budget impact of the intervention. This study did not include any benefits or costs associated with the other vitamins provided in the Healthy Start supplements (vitamin A, vitamin C and folic acid) (38). Further, the study took a local perspective and therefore did not include the costs of vitamins to the DH.

Salford CCG carried out a costing study [very serious limitations] with the aim of estimating the economic impact of universal supplementation of Healthy Start vitamins for all mothers during pregnancy and until their child is 12 months old and for all children under 4 years old in Salford. The study included operating costs of the scheme (such as licensing fee, consumables, facility and staff training), the cost of vitamins, and cost savings from avoidance of GP appointment and related test costs and from reducing the cost of treating rickets. The costs also included a publicity campaign to run in the first year of the programme with a top up fee in the two years following this (34).

The expected net costs of implementing the universal supplementation scheme are £73,932 for year 1, £37,063 for year 2, and £39,632 for year 3. The net cost in the first, second, and third year amounts, respectively, to £37,732, £36,063, and £38,632 without publicity campaign costs; £42,873, £46,053, and £52,337 if highest rate of uptake is achieved without publicity campaign costs; and £79,073, £47,053, and £53,337 if highest rate of uptake is achieved with publicity campaign costs (34).

This study was not a formal economic evaluation. This study did not include any benefits or costs associated with the other vitamins provided in the Healthy Start supplements (vitamin A, vitamin C and folic acid) (34). Further, the study took a local perspective and therefore did not include the costs of vitamins to the DH.

The figures reported in the included studies are not comparable with each other due to the different population sizes in each study. Per person costs were not reported in the majority of studies.

Evidence statement one – vitamin A

In the population groups of interest there was no evidence identified that investigated the cost-effectiveness of vitamin A supplementation.

Evidence statement two – vitamin C

In the population groups of interest there was no evidence identified that investigated the cost-effectiveness of vitamin C supplementation.

Evidence statement three – vitamin D

There is weak evidence from six [very serious limitations] cost studies and moderate evidence from one [minor limitations] economic evaluation (CEA) about the costs of providing supplementation with vitamin D. The studies rated with 'very serious limitations' were not formal economic evaluations.

Only one study[1] carried out extensive sensitivity analysis, though all studies included some scenario analysis. All of the studies included treatment costs associated with vitamin D only. Supplementation was often costed with Healthy Start supplements in mind; however, relevant cost savings associated with all the vitamins provided by Healthy Start supplements were not included. Only one study was a formal economic evaluation and many studies included crude estimates of costs.

The results of the studies are inconclusive. Of the seven studies identified, three found vitamin D supplementation to be cost saving and four found it to be cost incurring.

One study with moderate evidence[1] estimated that providing free supplements to the whole population of England and Wales resulted in an incremental cost of £4,086,142. The cost per symptomatic vitamin D deficiency averted was £2,859 for pregnant and breastfeeding women. The cost per symptomatic deficiency averted for children under 5 years was £1,229.

One study[2] estimated that the costs of providing free supplementation in Greater Manchester Primary Care Trust (PCT) to all pregnant women, breastfeeding women for one year postnatally and children up to 5 years (£2,336,475) is less than the cost of treating vitamin D deficiency (£4,248,322) even when 100% uptake is assumed. In scenarios with a lower uptake, the cost of supplementing would be less. Another study[3] estimated that the cost of supplying free vitamin supplements to 25% or less of the citywide population of pregnant women and up to 12 months postnatally and children under four years in Birmingham PCT (£164,988) is less than treating vitamin D deficiency (£165,000). However, with 100% uptake the cost of supplying vitamin D is estimated to be £659,952. A study by Lambeth CCG[4] found that the costs of supplying vitamins to pregnant women, breastfeeding mothers one year postnatally and children up to 4 years in Lambeth and Southwark (year 1 = £180,342, year 2 = £118,195) is less than the cost of treating vitamin D deficiency (£383,102). A study in Greater Manchester[5] estimated that the net cost (cost of intervention minus reduction in treatment costs) of supplying pregnant women and 12 months postnatally and children under four years would be £152,920, that is, no overall cost saving. A further study in the same setting and population groups in Salford[6] estimated the net costs to be £73,932 (year 1), £37,063 (year 2) and £29,632, this diminishes over time but still indicates no overall cost saving. A further study[7] which included the costs of treating vitamin D deficiency and the costs of supplying vitamins found that the costs of supplementing children under 5 years in Burnley Health Care Trust compared to no free supplements

being provided resulted in an incremental cost of supplying vitamin D according to COMA guidelines (supplementation for the first two years)* of £71,543 or £195,143 according to DH guidelines (supplementation for the first five years) at the time. It should be noted that the figures in the studies reported above are not comparable with each other due to the different population sizes in each study.

1 Filby *et al.,* 2014**
2 Turner *et al.,* 2012
3 McGee 2010
4 NHS Lambeth CCG, 2014
5 Salford CCG, 2013
6 Salford CCG, 2014
7 Zipitis *et al.,* 2006

* The reports refers to the following COMA report: Department of Health. Department of Health Report on Health and Social Subjects. 49 Nutrition and bone health with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food Policy. London: HMSO, 1998.

** In cases where reviewers were authors of an included study, data extraction and quality appraisal was undertaken by a reviewer completely independent to the study.

Evidence statement four – folic acid

In the population groups of interest there is moderate evidence from one study[1,] and weak evidence from one study[2].. One[1] [potentially serious limitations, partially applicable] economic evaluation on the cost-effectiveness of providing periconceptional supplementation of folic acid, compared to no folic acid supplementation in women planning a pregnancy and pregnant women and one[2] [very serious limitations, partially applicable] cost analysis of providing supplementation with multivitamins containined folic acid to pregnant women.

One study was carried out in a health-care setting in the Netherlands[1]. The study was appraised as having potential serious limitation mainly due to the lack of information reported. The authors did not fully report the model structure, resource use and units costs separately, cost sources and total cost, benefits were not reported separately and details about sensitivity analysis. The results showed that the incremental cost per discounted life-year gained through folic acid supplementation was £1,488.90. Univariate, multivariate and probabilistic sensitivity analyses were carried out. In the worst case scenario the cost per life year gained increased to £5,688.35; in the best case scenario the intervention was cost saving.

The second study was carried out in the US healthcare setting. The study was appraised as having very serious limitations as it was a cost analysis only and did not include health outcomes or any sensitivity analyses. The authors did not include all relevant costs. Providing supplementation with multivitamins containing folic acid to all pregnant women would cost £104 million and reducing the risk of NTDs and other conditions could prevent hospital charges of more the £832 million per year*.

1 Postma *et al.,* 2002
2 Bendich *et al.,* 1997

***** Please note that although this study included other conditions (low birth weight and cardiovascular birth defects) in the economic evaluation, these are not outcomes of interest as defined in the scope for this project.

3.3.2 Quality Assessment

As discussed in Section 3.3.1, all included studies were quality appraised as being partially applicable to the research question. Seven studies had very serious limitations, one had potentially serious limitations and one minor limitations. Due to the sparse evidence base in this area, studies with very serious limitations were included in the review. Those studies with 'very serious limitations' were not formal economic evaluations. Because the studies were not intended to be formal economic evaluations it is unsurprising that they score poorly on the economic evaluations quality appraisal checklist.

Issues that affected the applicability of included studies were not including the same relevant populations as the research question (and if they were included the results were not reported separately), not incorporating the value of health in results and not including costs and outcomes from other sectors.

Issues that affected the validity of included studies were often due to the studies not being full economic evaluations. Most were costing studies and so did not incorporate any measure of health benefits, did not describe a model structure, did not include health outcomes, did not provide an incremental analysis and did not include sensitivity analyses. Many studies also excluded a large number of relevant costs and only included the cost of buying the vitamins; many did not include resource use in the cost calculations.

The full results of quality appraisal are presented in Appendix E.

Section 4: Discussion

The review identified a small body of literature completed after 2002 that investigated the cost-effectiveness of the vitamins contained within the Healthy Start supplements. Due to the sparse evidence base, it was agreed that included studies from a cost-effectiveness review carried out for NICE Public Health maternal child and nutrition guidance (29) should be also be considered as many studies looking at the cost-effectiveness of folic acid would have been conducted in the 1990s. This was to enable search results showing the cost-effectiveness of folic acid supplementation pre-2000 to be considered, from which one relevant study in 1997 was identified. Further, those studies that were quality appraised as having very serious limitations were still included in the review. Those studies with 'very serious limitations' were not formal economic evaluations. Because the studies were not intended to be formal economic evaluations it is unsurprising that they score poorly on the economic evaluations quality appraisal checklist. These studies would usually be excluded from inclusion in the review.

Overall, nine studies were included in the review; all the studies were partially applicable to the research question. Seven studies had very serious limitations; one had potentially serious limitations and another had minor limitations. Two of the studies were formal economic evaluations, one CEA and one CCA. Of the seven studies with very serious limitations, none were formal economic evaluations and so did not incorporate any measure of health benefits, did not describe a model structure, did not include health outcomes, did not provide an incremental analysis and did not include sensitivity analyses. Further many studies gave crude estimates of costs and did not include all relevant costs with many not including resource use in the cost calculations. Because these studies were not intended to be formal economic evaluations it is unsurprising that they scored poorly on the economic evaluations quality appraisal checklist.

No studies were identified that evaluated the cost-effectiveness of Healthy Start supplements or of a similar multivitamin. All of the studies included in this review looked at individual nutrients.

No studies were identified that investigated the cost-effectiveness of vitamins A or C in the population groups relevant to this review.

One study included women planning a pregnancy and investigated folic acid supplementation (19). However, the study was conducted approximately 12 years ago in the Dutch healthcare system, and the study was also appraised as having potentially serious limitations. A second study also investigated folic acid supplementation, this study was conducted over 17 years ago in the US healthcare system, and the study was appraised as having very serious limitations. Therefore, it is difficult to draw firm conclusions on the cost-effectiveness of folic acid from these studies.

Seven studies investigated vitamin D supplementation in the remaining populations identified in Section 2.1.1. Of these, six studies included pregnant women, six studies included women with a child up to 12 months and seven studies included children up to the age of 5 years. All but one of these studies had very serious limitations and all but one of these studies reported results for all population groups together, rather than separate results by sub-group. Six of these studies were not formal economic evaluations but were cost analyses. Of these six studies, three found vitamin D supplementation to be cost saving and three found it to be cost incurring. It is difficult to draw conclusions from these studies due to the limitations with their methods. Many studies did not include all relevant costs and none of the studies included health benefits. One study carried out a formal economic evaluation (CCA) of the cost-effectiveness of vitamin D. This study also did not include health benefits. This study found providing universal supplementation of vitamin D in the whole eligible population to be cost-incurring. Due to the lack of data this study calculated the cost per case of symptomatic vitamin D deficiency averted. It is, therefore, difficult to say whether this is cost-effective as it does not calculate an ICER, which is the approach usually employed by NICE to determine cost-effectiveness. The heterogeneity observed in these results is likely to have been caused by the poor quality of many of the studies.

The studies that have been identified in this review do not answer the overarching question of this project, which is to examine the cost-effectiveness of moving the Healthy Start vitamin programme from the current targeted offering, to a universal offering. Although many studies did look at moving from a targeted to a universal approach of vitamin D supplementation, none of the studies looked at the benefits of other vitamins contained in the Healthy Start supplements. Further, all of the studies that looked at moving to a targeted approach were costing studies with a local perspective and were not formal economic evaluations. Therefore, in order to answer the overarching question an economic model will be developed.

4.1 LIMITATIONS AND GAPS IN THE EVIDENCE

Overall, relatively few studies were identified that helped answer the research question. There is the possibility that relevant literature was missed during the searches conducted for the review. However, an extensive search was conducted for the review which incorporated searching a range of electronic sources, citation searching, and reference checking of all studies reviewed at full paper stage and web-based search and a call for evidence. Furthermore, the criteria for study selection were very inclusive: they included studies with any of the vitamins of interest (it did not have to be the only vitamin the study was investigating), it also included any study type that may contain economic data and any study carried out in an OECD country. As a range of literature sources was searched and the inclusion criteria were inclusive it is unlikely that key studies were missed. Further, as the ERG pointed out that many studies investigating supplementation with folic acid may have been carried out in the 1990s, included studies from a cost-effectiveness review carried out for NICE Public Health maternal child and nutrition guidance (29) were also included in the review. The review therefore concluded that there is a lack of evidence investigating the cost-effectiveness of separate supplementation with folic acid, vitamin A, vitamin C and vitamin D, and particularly when these are taking in combination. The studies that have

been identified in this review do not answer the overarching question of this project, which is to examine the cost-effectiveness of moving the Healthy Start vitamin programme from the current targeted offering, to a universal offering. There were no studies identified that investigated Healthy Start supplements hence the inclusion of studies looking at single supplements.

The quality of studies identified in this review was poor. Studies that were quality appraised to be of poor quality had significant omissions that are very likely to change the results of the study. This means that it is not possible to have confidence in their reliability. This tended to be because the studies were local reports and could not be considered formal economic evaluations. However, all of the studies were partially applicable to the research questions: they all include a population group and vitamin of interest and the majority were conducted in the UK.

The majority of the evidence identified investigated vitamin D deficiency in pregnant women, women 1 year postnatally and children up to the age of four or five years. Although in many of the studies supplementation was provided with Healthy Start vitamins, the studies had an emphasis on vitamin D.

Due to the small evidence based of poor quality studies, caution needs to be applied when interpreting the results of these studies.

4.2 CONCLUSIONS

The majority of the evidence identified in this review investigated vitamin D deficiency in pregnant women, women 1 year postnatally and children up to the age of four or five years. Though in many of the studies supplementation was provided with Healthy Start vitamins, the studies had an emphasis on vitamin D and did not account for any benefits or costs associated with the other vitamin included in the Healthy Start supplement.

Due to the small evidence base of poor quality studies caution needs to be applied when interpreting the results of these studies. The result of this review suggests that further research is required into the cost-effectiveness of supplementation to women planning a pregnancy, pregnant women, women 12 months postnatally and children under 5 with the vitamins contained within the Healthy Start vitamin scheme. A formal economic evaluation of these vitamins would add to the evidence base.

The review shows that there are no cost-effectiveness studies already available to answer the overarching research question. However, some of the cost data identified in the review will be used to inform the economic model. Further, there are no cost-effectiveness studies from which the structure could be adapted and the model inputs updated. Therefore, it is necessary to build a *de novo* cost-effectiveness model to answer the overarching research question.

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APPENDIX A

PRISMA Checklist

Section/topic	#	Checklist item	Reported in Section
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Executive summary
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1.1 & 1.2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1.3 & 2.1
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2.1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2.2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix B
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2.3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2.4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	N/A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A

Section/topic	#	Checklist item	Reported in Section
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	3.1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 3.2. Appendix D
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix E
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Section 4
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	4.1
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4.2
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	This project has been funded by NICE

APPENDIX B

Search Strategy

1. Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Database name	MEDLINE and MEDLINE In-Process
Database host	Ovid SP
Database coverage dates	1946 to current (updated daily)
Searcher	Hannah Wood
Search date	18/09/14
Search strategy checked by	Mick Arber (information specialist YHEC), Paul Levay (information specialist NICE)
Number of records retrieved	1171
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	1171 (1170 to main Library, 1 direct to Duplicate Library)
Reference numbers of records in EndNote library	1-1170
Number of records after de-duplication in EndNote library	1167

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab,kf. (210)

2 exp Vitamin D/ec or exp Ascorbic Acid/ec or exp Folic Acid/ec or exp Vitamin A/ec or Vitamins/ec or Dietary Supplements/ec (447)

3 exp Vitamin D/sd or exp Ascorbic Acid/sd or exp Folic Acid/sd or exp Vitamin A/sd or Vitamins/sd or Dietary Supplements/sd (107)

4 or/1-3 (752)

5 vitamins/ or dietary supplements/ or food assistance/ (49142)

6 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,kf. (19253)

7 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,kf. (1575)

8 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (108119)

9 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab,kf. (1494)

10 exp Vitamin D/ or exp Vitamin D Deficiency/pc (45263)

11 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kf (384)

12 exp Ascorbic Acid/ or exp Ascorbic Acid Deficiency/pc (36108)

13 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kf. (1887)

14 exp Folic Acid/ or Folic Acid Deficiency/pc (29891)

15 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kf. (5926)

16 exp Vitamin A/ or Vitamin A Deficiency/pc (38235)

17 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kf. (1561)

18 or/5-17 (244210)

19 maternal welfare/ or maternal behavior/ or maternal health services/ or prenatal education/ (25056)

20 prenatal care/ or preconception care/ or postnatal care/ or perinatal care/ or postpartum period/ (44177)

21 pregnant women/ or pregnancy/ or breast feeding/ or pregnancy in adolescence/ or exp pregnancy outcome/ or pregnancy, unplanned/ or pregnancy, unwanted/ (727260)

22 Maternal Nutritional Physiological Phenomena/ (2221)

23 (mother$ or mum or mums or maternal$ or maternity or childbear$ or birth$ or pregnant or pregnanc$ or breastfeed$ or breast feed$ or breastfed$ or breast fed$ or lactating or lactation or conception or periconcept$ or preconcept$ or gestation$ or pregestation$ or perigestation$ or prenatal$ or pre-natal$ or perinatal$ or peri-natal$ or antenatal$ or ante-natal$ or postpartum or post-partum or postnatal$ or post-natal$ or puerperium or puerperal or parent$ or family or families or caregiver$ or care-giver$ or ((plan$ or try$ or attempt$) adj2 conceive)).ti,ab,kf. (1830005)

24 child/ or exp infant/ or child, preschool/ or exp pediatrics/ (2066323)

25 child welfare/ or exp child behavior/ or child health services/ or maternal-child health centers/ (52770)

26 child nutrition disorders/ or congenital abnormalities/ or exp neural tube defects/ or exp fetal development/ (129709)

27 (child$ or infant$ or infancy or toddler$ or neonate$ or neonatal$ or neo-nat$ or baby or babies or preschool$ or pre-school$ or pediatric$ or paediatric$ or newborn$ or new-born$ or kindergarten$ or nursery or nurseries or surestart or sure start or midwife$ or midwives or midwifery or health visitor$ or fetal or foetus$ or fetus$).ti,ab,kf. (1795548)

28 or/19-27 (4041796)

29 economics/ (27127)

30 exp "costs and cost analysis"/ (185059)

31 Economics, Dental/ (1867)
32 exp economics, hospital/ (19832)
33 Economics, Medical/ (8680)
34 Economics, Nursing/ (3985)
35 Economics, Pharmaceutical/ (2574)
36 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (484349)
37 (expenditure$ not energy).ti,ab. (19188)
38 value for money.ti,ab. (1018)
39 budget$.ti,ab. (19613)
40 or/29-39 (612983)
41 ((energy or oxygen) adj cost).ti,ab. (3004)
42 (metabolic adj cost).ti,ab. (867)
43 ((energy or oxygen) adj expenditure).ti,ab. (18032)
44 or/41-43 (21129)
45 40 not 44 (608270)
46 18 and 28 and 45 (1325)
47 4 or 46 (1984)
48 exp animals/ not humans/ (4011377)
49 (news or editorial or letter or comment or case reports).pt. (3056287)
50 case report.ti. (164355)
51 47 not (48 or 49 or 50) (1745)
52 limit 51 to (english language and yr="2000 -Current") (1223)
53 remove duplicates from 52 (1171)

2. Database: Embase <1974 to 2014 September 22>

Database name	**Embase**
Database host	Ovid SP
Database coverage dates	1974 to 22 September 2014
Searcher	Hannah Wood
Search date	23/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	1369
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	1369 (871 to main Library, 498 direct to Duplicate Library)
Reference numbers of records in EndNote library	1171-2041
Number of records after de-duplication in EndNote library	742

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab,kw. (254)

2 vitamin D/pe or ascorbic acid/pe or folic acid/pe or retinol/pe or vitamin/pe or multivitamin/pe (518)

3 1 or 2 (772)

4 *multivitamin/ or *prenatal formula/ or *vitamin mixture/ or *vitamin supplementation/ or *diet supplementation/ (26517)

5 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,kw. (24741)

6 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,kw. (1899)

7 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (128431)

8 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab,kw. (1947)

9 *vitamin D/ or *vitamin D deficiency/pc (18092)

10 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kw. (501)

11 *ascorbic acid/ or *ascorbic acid deficiency/pc (30617)

12 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kw. (2139)

13 *folic acid/ or *folic acid deficiency/pc (18364)

14 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kw. (7371)

15 *retinol/ or *retinol deficiency/pc (18235)

16 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,kw. (1730)

17 or/4-16 (199073)

18 maternal care/ or maternal welfare/ or maternal nutrition/ or maternal behavior/ or maternal attitude/ (40130)
19 prenatal care/ or postnatal care/ or exp puerperium/ or prenatal period/ or perinatal period/ or perinatal care/ (107808)
20 pregnant woman/ or exp pregnancy/ or breast feeding/ or pregnancy outcome/ (647337)
21 (mother$ or mum or mums or maternal$ or maternity or childbear$ or birth$ or pregnant or pregnanc$ or breastfeed$ or breast feed$ or breastfed$ or breast fed$ or lactating or lactation or conception or periconcept$ or preconcept$ or gestation$ or pregestation$ or perigestation$ or prenatal$ or pre-natal$ or perinatal$ or peri-natal$ or antenatal$ or ante-natal$ or postpartum or post-partum or postnatal$ or post-natal$ or puerperium or puerperal or parent or parents or parental or family or families or caregiver$ or care-giver$ or ((plan$ or try$ or attempt$) adj2 conceive)).ti,ab,kw. (2294231)
22 child/ or infant/ or preschool child/ or newborn period/ (1662211)
23 pediatrics/ (59226)
24 child health/ or child health care/ or early childhood intervention/ (47289)
25 child nutrition/ (12079)
26 exp neural tube defect/ (24159)
27 exp prenatal development/ (186716)
28 congenital disorder/ (71222)
29 (child$ or infant$ or infancy or toddler$ or neonate$ or neonatal$ or neo-nat$ or baby or babies or preschool$ or pre-school$ or pediatric$ or paediatric$ or newborn$ or new-born$ or kindergarten$ or nursery or nurseries or surestart or sure start or midwife$ or midwives or midwifery or health visitor$ or fetal or foetus$ or fetus$).ti,ab,kw. (2113932)
30 or/18-29 (4613441)
31 Health Economics/ (33836)
32 exp Economic Evaluation/ (215732)
33 exp Health Care Cost/ (208478)
34 pharmacoeconomics/ (5929)
35 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (624966)
36 (expenditure$ not energy).ti,ab. (24600)
37 (value adj2 money).ti,ab. (1426)
38 budget$.ti,ab. (24861)
39 or/31-38 (833981)
40 (metabolic adj cost).ti,ab. (924)
41 ((energy or oxygen) adj cost).ti,ab. (3206)
42 ((energy or oxygen) adj expenditure).ti,ab. (20760)
43 or/40-42 (24055)
44 39 not 43 (828803)
45 17 and 30 and 44 (1305)
46 3 or 45 (2031)
47 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (4868143)

48 animal/ or animal experiment/ or animal model/ or nonhuman/ (6311264)
49 exp human/ or human experiment/ (15133610)
50 (47 or 48) not 49 (5512081)
51 (letter or editorial or note).pt. (1882878)
52 46 not (50 or 51) (1802)
53 limit 52 to (english language and yr="2000 -Current") (1382)
54 remove duplicates from 53 (1369)

Note that the deep indexing in EMBASE meant that the EMTREE headings were very oversensitive. Headings focused after discussion with Paul Levay. Reduced the volume of records from over 1800 to 1369; scanning a sample of 200 of the records removed by introducing the focus suggested nothing of value was lost.

3. Database: AMED (Allied and Complementary Medicine) <1985 to September 2014>

Database name	AMED
Database host	Ovid SP
Database coverage dates	1985 to September 2014
Searcher	Hannah Wood
Search date	24/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	37
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	37 (35 to main Library, 2 direct to Duplicate Library)
Reference numbers of records in EndNote library	2042-2076
Number of records after de-duplication in EndNote library	30

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab. (1)

2 vitamins/ or dietary supplements/ (1855)

3 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (276)

4 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (31)

5 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (1684)

6 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab. (14)

7 ascorbic acid/ or vitamin a/ or folic acid/ or exp vitamin d/ (620)

8 exp deficiency disease/ (386)

9 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (6)

10 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (11)

11 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (41)

12 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (6)

13 or/2-12 (3034)

14 economics/ or exp "costs and cost analysis"/ (3624)

15 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (6473)

16 (expenditure$ not energy).ti,ab. (255)

17 value for money.ti,ab. (19)

18 budget$.ti,ab. (184)

19 or/14-18 (8648)

20 ((energy or oxygen) adj cost).ti,ab. (308)

21 (metabolic adj cost).ti,ab. (80)

22 ((energy or oxygen) adj expenditure).ti,ab. (494)

23 or/20-22 (809)

24 19 not 23 (8242)

25 13 and 24 (53)

26 1 or 25 (54)

27 limit 26 to (english and yr="2000 -Current") (37)

4. Database: Econlit <1886 to August 2014>

Database name	EconLit
Database host	Ovid SP
Database coverage dates	1886 to August 2014
Searcher	Hannah Wood
Search date	23/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	39
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	39 (35 to main Library, 4 direct to Duplicate Library)
Reference numbers of records in EndNote library	2007-2111
Number of records after de-duplication in EndNote library	34

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab. (4)

2 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (18)

3 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (45)

4 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (224)

5 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab. (17)

6 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (0)

7 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (0)

8 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (2)

9 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (0)

10 or/2-9 (294)

11 (mother$ or mum or mums or maternal$ or maternity or childbear$ or birth$ or pregnant or pregnanc$ or breastfeed$ or breast feed$ or breastfed$ or breast fed$ or lactating or lactation or conception or periconcept$ or preconcept$ or gestation$ or pregestation$ or perigestation$ or prenatal$ or pre-natal$ or perinatal$ or peri-natal$ or antenatal$ or ante-natal$ or postpartum or post-partum or postnatal$ or post-natal$ or puerperium or puerperal or parent$ or family or families or caregiver$ or care-giver$ or ((plan$ or try$ or attempt$) adj2 conceive)).ti,ab. (37511)

12 (child$ or infant$ or infancy or toddler$ or neonate$ or neonatal$ or neo-nat$ or baby or babies or preschool$ or pre-school$ or pediatric$ or paediatric$ or newborn$ or new-born$ or kindergarten$ or nursery or nurseries or surestart or sure start or midwife$ or midwives or midwifery or health visitor$ or fetal or foetus$ or fetus$).ti,ab. (20789)

13 or/11-12 (47538)

14 10 and 13 (47)

15 1 or 14 (51)

16 limit 15 to yr="2000 -Current" (39)

5. Database: HMIC Health Management Information Consortium <1979 to July 2014>

Database name	**HMIC**
Database host	Ovid SP
Database coverage dates	1979 to July 2014
Searcher	Hannah Wood
Search date	24/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	99
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	99 (95 to main Library, 4 direct to Duplicate Library)
Reference numbers of records in EndNote library	2112-2206
Number of records after de-duplication in EndNote library	67

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab. (76)
2 vitamins/ or dietary supplements/ or vitamin supplements/ (336)
3 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (197)
4 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab. (34)
5 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (810)
6 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab. (64)
7 exp Vitamin D deficiency/ or exp Vitamin D/ (208)
8 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (4)
9 vitamin c/ or exp vitamin c deficiency/ (39)
10 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (1)
11 Folic Acid/ (126)
12 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (63)
13 vitamin a/ or exp vitamin a deficiency/ (26)
14 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab. (1)
15 or/2-14 (1230)
16 exp economic analysis/ (1052)
17 exp "cost effectiveness"/ (5048)
18 exp costs/ (6317)
19 exp expenditure/ (7386)
20 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (32582)

21 (expenditure$ not energy).ti,ab. (3661)
22 value for money.ti,ab. (1056)
23 budget$.ti,ab. (4339)
24 or/16-23 (45673)
25 ((energy or oxygen) adj cost).ti,ab. (8)
26 (metabolic adj cost).ti,ab. (1)
27 ((energy or oxygen) adj expenditure).ti,ab. (100)
28 or/25-27 (108)
29 24 not 28 (45649)
30 1 or (15 and 29) (165)
31 limit 30 to (yr="2000 -Current" and english) (99)

6. Database: Social Policy and Practice <201407>

Database name	**Social Policy and Practice**
Database host	Ovid SP
Database coverage dates	1981 to July 2014
Searcher	Hannah Wood
Search date	24/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	43
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	43 (43 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	2207-2249
Number of records after de-duplication in EndNote library	32

1 (healthy start$ or healthystart$ or welfare food$ scheme$).ti,ab,de. (64)
2 ((vitamin$1 or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,de. (56)
3 ((supplement or supplements or supplementation) adj5 (provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ab,de. (31)
4 (vitamin$ or multivitamin$ or multi-micronutrient$ or multimicronutrient$ or multi-mineral$ or multimineral$ or multiple micronutrient$ or multiple micro-nutrient$ or multiple mineral$ or supplement or supplements or supplementation).ti. (735)
5 (pregnacare$ or pregna-care$ or sanatogen$ or centrum$ or seven sea$ or sevensea$ or pharmaton$ or vitabiotic$ or well woman$ or wellwoman$ or abidec$).ti,ab,de. (10)

6 ((vitaminD$1 or cholecalciferol$ or colecalciferol$ or ergocalciferol$ or calciferol$ or alfacalcidol$) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,de. (1)

7 ((vitaminC$1 or ascorbic$ or ascorbate or magnorbin or hybrin) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,de. (0)

8 ((vitaminB$1 or folic acid or folinic acid or folate or folacin$ or folvite or pteroylglutamic acid or pteroyl-l-glutam$ acid or pteroylmonoglutam$ or pteroylpolyglutamat$ or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,de. (9)

9 ((vitaminA$1 or retinoic acid or retinol or retinoids or retinyl or dehydroretinol or aquasol A) adj5 (supplement$ or provision or distribut$ or free$ or universal$ or means-test$ or income dependent$ or target$ or voucher$ or coupon$ or subsidy or subsidies or subsidis$ or subsidiz$ or discount$)).ti,ab,de. (0)

10 or/2-9 (805)

11 (mother$ or mum or mums or maternal$ or maternity or childbear$ or birth$ or pregnant or pregnanc$ or breastfeed$ or breast feed$ or breastfed$ or breast fed$ or lactating or lactation or conception or periconcept$ or preconcept$ or gestation$ or pregestation$ or perigestation$ or prenatal$ or pre-natal$ or perinatal$ or peri-natal$ or antenatal$ or ante-natal$ or postpartum or post-partum or postnatal$ or post-natal$ or puerperium or puerperal or parent$ or family or families or caregiver$ or care-giver$ or ((plan$ or try$ or attempt$) adj2 conceive)).ti,ab,de. (90559)

12 (child$ or infant$ or infancy or toddler$ or neonate$ or neonatal$ or neo-nat$ or baby or babies or preschool$ or pre-school$ or pediatric$ or paediatric$ or newborn$ or new-born$ or kindergarten$ or nursery or nurseries or surestart or sure start or midwife$ or midwives or midwifery or health visitor$ or fetal or foetus$ or fetus$).ti,ab,de. (130765)

13 11 or 12 (161573)

14 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab,de. (40077)

15 (expenditure$ not energy).ti,ab,de. (4719)

16 value for money.ti,ab,de. (1479)

17 budget$.ti,ab,de. (5312)

18 or/14-17 (47042)

19 ((energy or oxygen) adj cost).ti,ab,de. (11)

20 (metabolic adj cost).ti,ab,de. (0)

21 ((energy or oxygen) adj expenditure).ti,ab,de. (52)

22 or/19-21 (63)

23 18 not 22 (47000)

24 10 and 13 and 23 (49)

25 1 or 24 (112)

26 times educational supplement.ti. (264)

27 25 not 26 (88)
28 limit 27 to yr="2000 -Current" (43)

7. Database: Cochrane Database of Systematic Reviews (CDSR)

Database name	**Cochrane Database of Systematic Reviews CDSR**
Database host	Wiley
Database coverage dates	Issue 9 of 12 September 2014
Searcher	Hannah Wood
Search date	28/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	14
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	14 (14 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	2250-2263
Number of records after de-duplication in EndNote library	7

ID Search Hits
#1 (healthy next start* or healthystart* or welfare next food* next scheme*):ti,ab,kw 25
#2 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Economics - EC] 10
#3 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Supply & distribution - SD] 0
#4 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Economics - EC] 37
#5 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Supply & distribution - SD] 4
#6 MeSH descriptor: [Vitamin D] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 22
#7 MeSH descriptor: [Ascorbic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 0
#8 MeSH descriptor: [Folic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 34
#9 MeSH descriptor: [Vitamin A] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 9
#10 [or #1-#9] 135
#11 [mh ^vitamins] 1232
#12 [mh ^"dietary supplements"] 5976
#13 [mh ^"food assistance"] 4

#14 ((vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ab,kw 3577

#15 ((supplement or supplements or supplementation) near/5 (provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ab,kw 316

#16 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral* or supplement or supplements or supplementation):ti 15750

#17 (pregnacare* or pregna next care* or sanatogen* or centrum* or seven next sea* or sevensea* or pharmaton* or vitabiotic* or well next woman* or wellwoman* or abidec*):ti,ab,kw 97

#18 [mh "vitamin d"] 2347

#19 MeSH descriptor: [Vitamin D Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 117

#20 ((vitaminD* or cholecalciferol* or colecalciferol* or ergocalciferol* or calciferol* or alfacalcidol*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ti,ab,kw 234

#21 [mh "ascorbic acid"] 1544

#22 MeSH descriptor: [Ascorbic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 1

#23 ((vitaminC* or ascorbic* or ascorbate or magnorbin or hybrin) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ti,ab,kw 237

#24 [mh "folic acid"] 2234

#25 MeSH descriptor: [Folic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 22

#26 ((vitaminB* or "folic acid" or "folinic acid" or folate or folacin* or folvite or "pteroylglutamic acid" or pteroyl next l next glutam* next acid or pteroylmonoglutam* or pteroylpolyglutamat* or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ti,ab,kw 891

#27 [mh "vitamin a"] 1562

#28 MeSH descriptor: [Vitamin A Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 73

#29 ((vitaminA* or "retinoic acid" or retinol or retinoids or retinyl or dehydroretinol or "aquasol A") near/5 (supplement* or provision or distribut* or free* or universal* or

means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*)):ti,ab,kw 146

#30 [or #11-#29] 22781

#31 [mh ^"maternal welfare"] or [mh ^"maternal behavior"] or [mh ^"maternal health services"] or [mh ^"prenatal education"] 499

#32 [mh ^"prenatal care"] or [mh ^"preconception care"] or [mh ^"postnatal care"] or [mh ^"perinatal care"] or [mh ^"postpartum period"] 2082

#33 [mh ^"pregnant women"] or [mh ^pregnancy] or [mh ^"breast feeding"] or [mh ^"pregnancy in adolescence"] or [mh "pregnancy outcome"] or [mh ^"pregnancy, unplanned"] or [mh ^"pregnancy, unwanted"] 4383

#34 [mh ^"Maternal Nutritional Physiological Phenomena"] 106

#35 (mother* or mum or mums or maternal* or maternity or childbear* or birth* or pregnant or pregnanc* or breastfeed* or breast next feed* or breastfed* or breast next fed* or lactating or lactation or conception or periconcept* or preconcept* or gestation* or pregestation* or perigestation* or prenatal* or pre next natal* or perinatal* or peri next natal* or antenatal* or ante next natal* or postpartum or post next partum or postnatal* or post next natal* or puerperium or puerperal or parent or parents or parental or family or families or caregiver* or care next giver* or ((plan* or try* or attempt*) near/2 conceive)):ti,ab,kw 66851

#36 [mh ^child] or [mh infant] or [mh ^"child, preschool"] or [mh pediatrics] or [mh ^"child welfare"] or [mh "child behavior"] or [mh ^"child health services"] or [mh ^"maternal-child health centres"] 15113

#37 [mh ^"child nutrition disorders"] or [mh "neural tube defects"] or [mh "fetal development"] or [mh ^"congenital abnormalities"] 2396

#38 (child* or infant* or infancy or toddler* or neonate* or neonatal* or neo next nat* or baby or babies or preschool* or pre next school* or pediatric* or paediatric* or newborn* or new next born* or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or health next visitor* or fetal or foetus* or fetus*):ti,ab,kw 103185

#39 [or #31-#38] 138159

#40 [mh ^economics] 57

#41 [mh "costs and cost analysis"] 22632

#42 [mh ^"economics, dental"] or [mh "economics, hospital"] or [mh ^"economics, medical"] or [mh ^"economics, nursing"] or [mh ^"economics, pharmaceutical"] 1917

#43 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*):ti,ab,kw 44091

#44 (expenditure* not energy):ti,ab,kw 891

#45 ("value for money"):ti,ab,kw 78

#46 (budget*):ti,ab,kw 365

#47 [or #40-#46] 44548

#48 ((energy or oxygen) next cost):ti,ab,kw 262

#49 (metabolic next cost):ti,ab,kw 67

#50 ((energy or oxygen) next expenditure):ti,ab,kw 1909

#51 [or #48-#50] 2150

#52 #47 not #51 44179

#53 (#30 and #39 and #52) or #10 297
#54 #53 Publication Year from 2000 to 2014, in Cochrane Reviews (Reviews and Protocols) 14

8. Database: Cochrane Central Register of Controlled Trials (CENTRAL)

Database name	**Cochrane Central Register of Controlled Trials (CENTRAL)**
Database host	Wiley
Database coverage dates	Issue 8 of 12 August 2014
Searcher	Hannah Wood
Search date	28/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	160
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	160 (158 to main Library, 2 direct to Duplicate Library)
Reference numbers of records in EndNote library	2264-2421
Number of records after de-duplication in EndNote library	36

ID Search Hits
#1 healthy next start* or healthystart* or welfare next food* next scheme* 32
#2 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Economics - EC] 10
#3 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Supply & distribution - SD] 0
#4 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Economics - EC] 37
#5 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Supply & distribution - SD] 4
#6 MeSH descriptor: [Vitamin D] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 22
#7 MeSH descriptor: [Ascorbic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 0
#8 MeSH descriptor: [Folic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 34
#9 MeSH descriptor: [Vitamin A] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 9
#10 [or #1-#9] 142
#11 [mh ^vitamins] 1232
#12 [mh ^"dietary supplements"] 5976
#13 [mh ^"food assistance"] 4

#14 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 4571

#15 (supplement or supplements or supplementation) near/5 (provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 476

#16 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral* or supplement or supplements or supplementation):ti 15750

#17 pregnacare* or pregna next care* or sanatogen* or centrum* or seven next sea* or sevensea* or pharmaton* or vitabiotic* or well next woman* or wellwoman* or abidec* 584

#18 [mh "vitamin d"] 2347

#19 MeSH descriptor: [Vitamin D Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 117

#20 (vitaminD* or cholecalciferol* or colecalciferol* or ergocalciferol* or calciferol* or alfacalcidol*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 245

#21 [mh "ascorbic acid"] 1544

#22 MeSH descriptor: [Ascorbic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 1

#23 (vitaminC* or ascorbic* or ascorbate or magnorbin or hybrin) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 247

#24 [mh "folic acid"] 2234

#25 MeSH descriptor: [Folic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 22

#26 (vitaminB* or "folic acid" or "folinic acid" or folate or folacin* or folvite or "pteroylglutamic acid" or pteroyl next l next glutam* next acid or pteroylmonoglutam* or pteroylpolyglutamat* or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 986

#27 [mh "vitamin a"] 1562

#28 MeSH descriptor: [Vitamin A Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 73

#29 (vitaminA* or "retinoic acid" or retinol or retinoids or retinyl or dehydroretinol or "aquasol A") near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 159

#30 [or #11-#29] 23591

#31 [mh ^"maternal welfare"] or [mh ^"maternal behavior"] or [mh ^"maternal health services"] or [mh ^"prenatal education"] 499

#32 [mh ^"prenatal care"] or [mh ^"preconception care"] or [mh ^"postnatal care"] or [mh ^"perinatal care"] or [mh ^"postpartum period"] 2082

#33 [mh ^"pregnant women"] or [mh ^pregnancy] or [mh ^"breast feeding"] or [mh ^"pregnancy in adolescence"] or [mh "pregnancy outcome"] or [mh ^"pregnancy, unplanned"] or [mh ^"pregnancy, unwanted"] 4383

#34 [mh ^"Maternal Nutritional Physiological Phenomena"] 106

#35 mother* or mum or mums or maternal* or maternity or childbear* or birth* or pregnant or pregnanc* or breastfeed* or breast next feed* or breastfed* or breast next fed* or lactating or lactation or conception or periconcept* or preconcept* or gestation* or pregestation* or perigestation* or prenatal* or pre next natal* or perinatal* or peri next natal* or antenatal* or ante next natal* or postpartum or post next partum or postnatal* or post next natal* or puerperium or puerperal or parent or parents or parental or family or families or caregiver* or care next giver* or ((plan* or try* or attempt*) near/2 conceive) 78237

#36 [mh ^child] or [mh infant] or [mh ^"child, preschool"] or [mh pediatrics] or [mh ^"child welfare"] or [mh "child behavior"] or [mh ^"child health services"] or [mh ^"maternal-child health centres"] 15113

#37 [mh ^"child nutrition disorders"] or [mh "neural tube defects"] or [mh "fetal development"] or [mh ^"congenital abnormalities"] 2396

#38 child* or infant* or infancy or toddler* or neonate* or neonatal* or neo next nat* or baby or babies or preschool* or pre next school* or pediatric* or paediatric* or newborn* or new next born* or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or health next visitor* or fetal or foetus* or fetus* 116727

#39 [or #31-#38] 155704

#40 [mh ^economics] 57

#41 [mh "costs and cost analysis"] 22632

#42 [mh ^"economics, dental"] or [mh "economics, hospital"] or [mh ^"economics, medical"] or [mh ^"economics, nursing"] or [mh ^"economics, pharmaceutical"] 1917

#43 economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* 62202

#44 expenditure* not energy 1532

#45 "value for money" 314

#46 budget* 895

#47 [or #40-#46] 62582

#48 (energy or oxygen) next cost 289

#49 metabolic next cost 72

#50 (energy or oxygen) next expenditure 2086
#51 [or #48-#50] 2349
#52 #47 not #51 62056
#53 (#30 and #39 and #52) or #10 706
#54 #53 Publication Year from 2000 to 2014, in Trials 160

9. Database: Database of Abstracts of Reviews of Effectiveness (DARE)

Database name	**Database of Abstracts of Reviews of Effectiveness (DARE)**
Database host	Wiley
Database coverage dates	Issue 3 of 4 July 2014
Searcher	Hannah Wood
Search date	28/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	87
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	87 (87 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	2422-2508
Number of records after de-duplication in EndNote library	82

ID Search Hits
#1 healthy next start* or healthystart* or welfare next food* next scheme* 32
#2 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Economics - EC] 10
#3 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Supply & distribution - SD] 0
#4 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Economics - EC] 37
#5 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Supply & distribution - SD] 4
#6 MeSH descriptor: [Vitamin D] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 22
#7 MeSH descriptor: [Ascorbic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 0
#8 MeSH descriptor: [Folic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 34
#9 MeSH descriptor: [Vitamin A] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 9
#10 [or #1-#9] 142
#11 [mh ^vitamins] 1232
#12 [mh ^"dietary supplements"] 5976

#13 [mh ^"food assistance"] 4

#14 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 4571

#15 (supplement or supplements or supplementation) near/5 (provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 476

#16 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral* or supplement or supplements or supplementation):ti 15750

#17 pregnacare* or pregna next care* or sanatogen* or centrum* or seven next sea* or sevensea* or pharmaton* or vitabiotic* or well next woman* or wellwoman* or abidec* 584

#18 [mh "vitamin d"] 2347

#19 MeSH descriptor: [Vitamin D Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 117

#20 (vitaminD* or cholecalciferol* or colecalciferol* or ergocalciferol* or calciferol* or alfacalcidol*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 245

#21 [mh "ascorbic acid"] 1544

#22 MeSH descriptor: [Ascorbic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 1

#23 (vitaminC* or ascorbic* or ascorbate or magnorbin or hybrin) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 247

#24 [mh "folic acid"] 2234

#25 MeSH descriptor: [Folic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 22

#26 (vitaminB* or "folic acid" or "folinic acid" or folate or folacin* or folvite or "pteroylglutamic acid" or pteroyl next l next glutam* next acid or pteroylmonoglutam* or pteroylpolyglutamat* or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 986

#27 [mh "vitamin a"] 1562

#28 MeSH descriptor: [Vitamin A Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 73

#29 (vitaminA* or "retinoic acid" or retinol or retinoids or retinyl or dehydroretinol or "aquasol A") near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 159

#30 [or #11-#29] 23591

#31 [mh ^"maternal welfare"] or [mh ^"maternal behavior"] or [mh ^"maternal health services"] or [mh ^"prenatal education"] 499

#32 [mh ^"prenatal care"] or [mh ^"preconception care"] or [mh ^"postnatal care"] or [mh ^"perinatal care"] or [mh ^"postpartum period"] 2082

#33 [mh ^"pregnant women"] or [mh ^pregnancy] or [mh ^"breast feeding"] or [mh ^"pregnancy in adolescence"] or [mh "pregnancy outcome"] or [mh ^"pregnancy, unplanned"] or [mh ^"pregnancy, unwanted"] 4383

#34 [mh ^"Maternal Nutritional Physiological Phenomena"] 106

#35 mother* or mum or mums or maternal* or maternity or childbear* or birth* or pregnant or pregnanc* or breastfeed* or breast next feed* or breastfed* or breast next fed* or lactating or lactation or conception or periconcept* or preconcept* or gestation* or pregestation* or perigestation* or prenatal* or pre next natal* or perinatal* or peri next natal* or antenatal* or ante next natal* or postpartum or post next partum or postnatal* or post next natal* or puerperium or puerperal or parent or parents or parental or family or families or caregiver* or care next giver* or ((plan* or try* or attempt*) near/2 conceive) 78237

#36 [mh ^child] or [mh infant] or [mh ^"child, preschool"] or [mh pediatrics] or [mh ^"child welfare"] or [mh "child behavior"] or [mh ^"child health services"] or [mh ^"maternal-child health centres"] 15113

#37 [mh ^"child nutrition disorders"] or [mh "neural tube defects"] or [mh "fetal development"] or [mh ^"congenital abnormalities"] 2396

#38 child* or infant* or infancy or toddler* or neonate* or neonatal* or neo next nat* or baby or babies or preschool* or pre next school* or pediatric* or paediatric* or newborn* or new next born* or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or health next visitor* or fetal or foetus* or fetus* 116727

#39 [or #31-#38] 155704

#40 [mh ^economics] 57

#41 [mh "costs and cost analysis"] 22632

#42 [mh ^"economics, dental"] or [mh "economics, hospital"] or [mh ^"economics, medical"] or [mh ^"economics, nursing"] or [mh ^"economics, pharmaceutical"] 1917

#43 economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* 62202

#44 expenditure* not energy 1532

#45 "value for money" 314

#46 budget* 895

#47 [or #40-#46] 62582

#48 (energy or oxygen) next cost 289

#49 metabolic next cost 72

#50 (energy or oxygen) next expenditure 2086
#51 [or #48-#50] 2349
#52 #47 not #51 62056
#53 (#30 and #39 and #52) or #10 706
#54 #53 Publication Year from 2000 to 2014, in Other Reviews 87

10. Database: Health Technology Assessment Database (HTA Database)

Database name	**Health Technology Assessment Database (HTA Database)**
Database host	Wiley
Database coverage dates	Issue 3 of 4 July 2014
Searcher	Hannah Wood
Search date	28/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	22
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	22 (22 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	2509-2530
Number of records after de-duplication in EndNote library	19

ID Search Hits
#1 healthy next start* or healthystart* or welfare next food* next scheme* 32
#2 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Economics - EC] 10
#3 MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Supply & distribution - SD] 0
#4 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Economics - EC] 37
#5 MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Supply & distribution - SD] 4
#6 MeSH descriptor: [Vitamin D] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 22
#7 MeSH descriptor: [Ascorbic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 0
#8 MeSH descriptor: [Folic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 34
#9 MeSH descriptor: [Vitamin A] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 9
#10 [or #1-#9] 142
#11 [mh ^vitamins] 1232
#12 [mh ^"dietary supplements"] 5976

#13 [mh ^"food assistance"] 4

#14 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 4571

#15 (supplement or supplements or supplementation) near/5 (provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 476

#16 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral* or supplement or supplements or supplementation):ti 15750

#17 pregnacare* or pregna next care* or sanatogen* or centrum* or seven next sea* or sevensea* or pharmaton* or vitabiotic* or well next woman* or wellwoman* or abidec* 584

#18 [mh "vitamin d"] 2347

#19 MeSH descriptor: [Vitamin D Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 117

#20 (vitaminD* or cholecalciferol* or colecalciferol* or ergocalciferol* or calciferol* or alfacalcidol*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 245

#21 [mh "ascorbic acid"] 1544

#22 MeSH descriptor: [Ascorbic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 1

#23 (vitaminC* or ascorbic* or ascorbate or magnorbin or hybrin) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 247

#24 [mh "folic acid"] 2234

#25 MeSH descriptor: [Folic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 22

#26 (vitaminB* or "folic acid" or "folinic acid" or folate or folacin* or folvite or "pteroylglutamic acid" or pteroyl next l next glutam* next acid or pteroylmonoglutam* or pteroylpolyglutamat* or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 986

#27 [mh "vitamin a"] 1562

#28 MeSH descriptor: [Vitamin A Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 73

#29 (vitaminA* or "retinoic acid" or retinol or retinoids or retinyl or dehydroretinol or "aquasol A") near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 159

#30 [or #11-#29] 23591

#31 [mh ^"maternal welfare"] or [mh ^"maternal behavior"] or [mh ^"maternal health services"] or [mh ^"prenatal education"] 499

#32 [mh ^"prenatal care"] or [mh ^"preconception care"] or [mh ^"postnatal care"] or [mh ^"perinatal care"] or [mh ^"postpartum period"] 2082

#33 [mh ^"pregnant women"] or [mh ^pregnancy] or [mh ^"breast feeding"] or [mh ^"pregnancy in adolescence"] or [mh "pregnancy outcome"] or [mh ^"pregnancy, unplanned"] or [mh ^"pregnancy, unwanted"] 4383

#34 [mh ^"Maternal Nutritional Physiological Phenomena"] 106

#35 mother* or mum or mums or maternal* or maternity or childbear* or birth* or pregnant or pregnanc* or breastfeed* or breast next feed* or breastfed* or breast next fed* or lactating or lactation or conception or periconcept* or preconcept* or gestation* or pregestation* or perigestation* or prenatal* or pre next natal* or perinatal* or peri next natal* or antenatal* or ante next natal* or postpartum or post next partum or postnatal* or post next natal* or puerperium or puerperal or parent or parents or parental or family or families or caregiver* or care next giver* or ((plan* or try* or attempt*) near/2 conceive) 78237

#36 [mh ^child] or [mh infant] or [mh ^"child, preschool"] or [mh pediatrics] or [mh ^"child welfare"] or [mh "child behavior"] or [mh ^"child health services"] or [mh ^"maternal-child health centres"] 15113

#37 [mh ^"child nutrition disorders"] or [mh "neural tube defects"] or [mh "fetal development"] or [mh ^"congenital abnormalities"] 2396

#38 child* or infant* or infancy or toddler* or neonate* or neonatal* or neo next nat* or baby or babies or preschool* or pre next school* or pediatric* or paediatric* or newborn* or new next born* or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or health next visitor* or fetal or foetus* or fetus* 116727

#39 [or #31-#38] 155704

#40 #10 or (#30 and #39) 6867

#41 #40 Publication Year from 2000 to 2014, in Technology Assessments 22

11. Database: NHS Economic Evaluation Database (NHS EED)

Database name	**NHS Economic Evaluation Database (NHS EED)**
Database host	Wiley
Database coverage dates	Issue 3 of 4 July 2014
Searcher	Hannah Wood
Search date	28/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	88
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	88 (88 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	2531-2618
Number of records after de-duplication in EndNote library	18

ID	Search Hits
#1	healthy next start* or healthystart* or welfare next food* next scheme* 32
#2	MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Economics - EC] 10
#3	MeSH descriptor: [Vitamins] this term only and with qualifier(s): [Supply & distribution - SD] 0
#4	MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Economics - EC] 37
#5	MeSH descriptor: [Dietary Supplements] this term only and with qualifier(s): [Supply & distribution - SD] 4
#6	MeSH descriptor: [Vitamin D] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 22
#7	MeSH descriptor: [Ascorbic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 0
#8	MeSH descriptor: [Folic Acid] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 34
#9	MeSH descriptor: [Vitamin A] explode all trees and with qualifier(s): [Economics - EC, Supply & distribution - SD] 9
#10	[or #1-#9] 142
#11	[mh ^vitamins] 1232
#12	[mh ^"dietary supplements"] 5976
#13	[mh ^"food assistance"] 4
#14	(vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 4571

#15 (supplement or supplements or supplementation) near/5 (provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 476

#16 (vitamin* or multivitamin* or multi next micronutrient* or multimicronutrient* or multi next mineral* or multimineral* or multiple next micronutrient* or multiple next micro next nutrient* or multiple next mineral* or supplement or supplements or supplementation):ti 15750

#17 pregnacare* or pregna next care* or sanatogen* or centrum* or seven next sea* or sevensea* or pharmaton* or vitabiotic* or well next woman* or wellwoman* or abidec* 584

#18 [mh "vitamin d"] 2347

#19 MeSH descriptor: [Vitamin D Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 117

#20 (vitaminD* or cholecalciferol* or colecalciferol* or ergocalciferol* or calciferol* or alfacalcidol*) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 245

#21 [mh "ascorbic acid"] 1544

#22 MeSH descriptor: [Ascorbic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 1

#23 (vitaminC* or ascorbic* or ascorbate or magnorbin or hybrin) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 247

#24 [mh "folic acid"] 2234

#25 MeSH descriptor: [Folic Acid Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 22

#26 (vitaminB* or "folic acid" or "folinic acid" or folate or folacin* or folvite or "pteroylglutamic acid" or pteroyl next l next glutam* next acid or pteroylmonoglutam* or pteroylpolyglutamat* or methyltetrahydrofolate or dihydrofolate or methylfolate or tetrahydrofolate) near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 986

#27 [mh "vitamin a"] 1562

#28 MeSH descriptor: [Vitamin A Deficiency] explode all trees and with qualifier(s): [Prevention & control - PC] 73

#29 (vitaminA* or "retinoic acid" or retinol or retinoids or retinyl or dehydroretinol or "aquasol A") near/5 (supplement* or provision or distribut* or free* or universal* or means next test* or income next dependent* or target* or voucher* or coupon* or subsidy or subsidies or subsidis* or subsidiz* or discount*) 159

#30 [or #11-#29] 23591

#31 [mh ^"maternal welfare"] or [mh ^"maternal behavior"] or [mh ^"maternal health services"] or [mh ^"prenatal education"] 499

#32 [mh ^"prenatal care"] or [mh ^"preconception care"] or [mh ^"postnatal care"] or [mh ^"perinatal care"] or [mh ^"postpartum period"] 2082

#33 [mh ^"pregnant women"] or [mh ^pregnancy] or [mh ^"breast feeding"] or [mh ^"pregnancy in adolescence"] or [mh "pregnancy outcome"] or [mh ^"pregnancy, unplanned"] or [mh ^"pregnancy, unwanted"] 4383

#34 [mh ^"Maternal Nutritional Physiological Phenomena"] 106

#35 mother* or mum or mums or maternal* or maternity or childbear* or birth* or pregnant or pregnanc* or breastfeed* or breast next feed* or breastfed* or breast next fed* or lactating or lactation or conception or periconcept* or preconcept* or gestation* or pregestation* or perigestation* or prenatal* or pre next natal* or perinatal* or peri next natal* or antenatal* or ante next natal* or postpartum or post next partum or postnatal* or post next natal* or puerperium or puerperal or parent or parents or parental or family or families or caregiver* or care next giver* or ((plan* or try* or attempt*) near/2 conceive) 78237

#36 [mh ^child] or [mh infant] or [mh ^"child, preschool"] or [mh pediatrics] or [mh ^"child welfare"] or [mh "child behavior"] or [mh ^"child health services"] or [mh ^"maternal-child health centres"] 15113

#37 [mh ^"child nutrition disorders"] or [mh "neural tube defects"] or [mh "fetal development"] or [mh ^"congenital abnormalities"] 2396

#38 child* or infant* or infancy or toddler* or neonate* or neonatal* or neo next nat* or baby or babies or preschool* or pre next school* or pediatric* or paediatric* or newborn* or new next born* or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or health next visitor* or fetal or foetus* or fetus* 116727

#39 [or #31-#38] 155704

#40 #10 or (#30 and #39) 6867

#41 #40 Publication Year from 2000 to 2014, in Economic Evaluations 88

12. Database: Cost Effectiveness Registry (CEA Registry)

Database name	CEA Registry
Database host	https://research.tufts-nemc.org/cear4/
Database coverage dates	1976 - Last update 2013
Searcher	Hannah Wood
Search date	29/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	0
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	0
Reference numbers of records in EndNote library	N/A
Number of records after de-duplication in EndNote library	0

CEA (basic, non-subscription access) only allows one search term to be entered at a time and there are no options to export search results. Returned records were screened in the database and only those that appeared to be potentially relevant were added to EndNote. Potentially relevant records were not added to EndNote if the citation had been identified by another database and previously downloaded.

Terms:

Healthy Start
HealthyStart
Vitamin
Vitamins
Supplement
Supplements
Supplementation
Multivitamin
Multivitamins
Multi-vitamin
Multi-vitamins
Multimineral
Multiminerals
Multi-mineral
Multi-minerals
Micronutrient
Micronutrients
Micro-nutrient
Micro-nutrients
Multimicronutrient
Multimicronutrients
Multi-micronutrient

Multi-micronutrients
Pregnacare
Sanatogen
Centrum
Seven Seas
Pharmaton
Vitabiotic
Abidec
Well woman
VitaminD
Cholecalciferol
Ergocalciferol
Calciferol
Alfacalcidol
VitaminC
Ascorbic
Ascorbate
Magnorbin
Hybrin
VitaminB
Folic acid
Folinic acid
Folate
Folacin
Folvite
vitaminA
Retinoic acid
Retinol
Retinoids
Retinyl
Dehydroretinol
Aquasol

0 new records added to EndNote

13. Database: ASSIA (Applied Social Science Index and Abstracts)

Database name	**ASSIA (Applied Social Science Index and Abstracts)**
Database host	Proquest
Database coverage dates	1987 – current. No information on date of last update provided.
Searcher	Hannah Wood
Search date	29/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	524
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	524 (410 to main Library, 114 direct to Duplicate Library)
Reference numbers of records in EndNote library	2619-3028
Number of records after de-duplication in EndNote library	366

Problem with Proquest interface meant that it was not possible to undertake complex multi-line searches; the database kept timing out and would not combine separate lines with Boolean operators. Proquest support could not suggest anything more than simplifying the search strategy. Basic searches undertaken, for the vitamin concept only, downloaded one search-line at a time as the interface crashed when trying to combine lines with OR.

TI,AB("healthy start*" OR healthystart* OR "welfare food* scheme*")
Date: From 2000 to 2014

39 results

SU.EXACT("Vitamin A supplement") OR SU.EXACT("Vitamin D supplement") OR SU.EXACT("Vitamin C") OR SU.EXACT("Folic acid supplement") OR SU.EXACT("Vitamin supplements") OR SU.EXACT("Food supplements")
Date: From 2000 to 2014

159 results

TI,AB((vitamin* OR multivitamin* OR "multi-micronutrient*" OR multimicronutrient* OR "multi-mineral*" OR multimineral* OR "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*") NEAR/5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

219 results

TI,AB((supplement OR supplements OR supplementation) NEAR/5 (provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

33 results

TI,AB((vitaminD* OR cholecalciferol* OR colecalciferol* OR ergocalciferol* OR calciferol* OR alfacalcidol*) NEAR/5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

8 results

TI,AB((vitaminC* OR ascorbic* OR ascorbate OR magnorbin OR hybrin) NEAR/5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

0 results

TI,AB((vitaminB* OR "folic acid" OR "folinic acid" OR folate OR folacin* OR folvite OR "pteroylglutamic acid" OR “pteroyl l glutam* acid” OR pteroylmonoglutam* OR pteroylpolyglutamat* OR methyltetrahydrofolate OR dihydrofolate OR methylfolate OR tetrahydrofolate) NEAR/5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

59 results

TI,AB(vitaminA* OR "retinoic acid" OR retinol OR retinoids OR retinyl OR dehydroretinol OR "aquasol A") NEAR/5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))
Date: From 2000 to 2014

5 results

TI,AB((wellwoman* OR "well woman*") AND (vitamin* OR supplement*))
Date: From 2000 to 2014

0 results

TI,AB(pregnacare* OR sanatogen* OR centrum* OR "seven seas" OR sevenseas* OR pharmaton* OR vitabiotic* OR abidec*)
Date: From 2000 to 2014

2 results

14. Database: Health Economic Evaluation Databases (HEED)

Database name	**Health Economic Evaluation Databases (HEED)**
Database host	EBSCO
Database coverage dates	1983-2014
Searcher	Hannah Wood
Search date	29/09/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	48
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	48 (47 to main Library, 1 direct to Duplicate Library)
Reference numbers of records in EndNote library	3029-3075
Number of records after de-duplication in EndNote library	10

S17 S1 OR S15 Limiters - Published Date: 20000101-20141231 48
S16 S1 OR S15 71
S15 S13 AND S14 71
S14 S11 OR S12 8,837
S13 S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 250
S12 TX(child* or infant* or infancy or toddler* or neonate* or neonatal* or “neo nat*” or baby or babies or preschool* or “pre school*” or pediatric* or paediatric* or newborn* or “new born*” or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or “health visitor*” or fetal or foetus* or fetus*) 6,356
S11 TX(mother* OR mum OR mums OR maternal* OR maternity OR childbear* OR birth* OR pregnant OR pregnanc* OR breastfeed* OR “breast feed*” OR breastfed* OR “breast fed*” OR lactating OR lactation OR conception OR periconcept* OR preconcept* OR gestation* OR pregestation* OR perigestation* OR prenatal* OR “pre natal*” OR perinatal* OR “peri natal*” OR antenatal* OR “ante natal*” OR postpartum OR “post partum” OR postnatal* OR “post natal*” OR puerperium OR puerperal OR parent OR parents OR parental OR family OR families OR caregiver* OR “care giver*” OR ((plan* OR try* OR attempt*) N2 conceive)) 4,453

S10	TX(vitaminA* OR "retinoic acid" OR retinol OR retinoids OR retinyl OR dehydroretinol OR "aquasol A")	10
S9	TX(vitaminB* OR "folic acid" OR "folinic acid" OR folate OR folacin* OR folvite OR "pteroylglutamic acid" OR “pteroyl l glutam* acid” OR pteroylmonoglutam* OR pteroylpolyglutamat* OR methyltetrahydrofolate OR dihydrofolate OR methylfolate OR tetrahydrofolate)	64
S8	TX(vitaminC* OR ascorbic* OR ascorbate OR magnorbin OR hybrin)	4
S7	TX(vitaminD* OR cholecalciferol* OR colecalciferol* OR ergocalciferol* OR calciferol* OR alfacalcidol*)	18
S6	TX((wellwoman* OR "well woman*") AND (vitamin* OR supplement*))	0
S5	TX(pregnacare* OR sanatogen* OR centrum* OR "seven seas" OR sevenseas* OR pharmaton* OR vitabiotic* OR abidec*)	1
S4	TI(vitamin* OR multivitamin* OR "multi-micronutrient*" OR multimicronutrient* OR "multi-mineral*" OR multimineral* OR "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*" OR supplement OR supplements OR supplementation)	148
S3	TX((supplement OR supplements OR supplementation) N5 (provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	6
S2	TX((vitamin* OR multivitamin* OR "multi-micronutrient*" OR multimicronutrient* OR "multi-mineral*" OR multimineral* OR "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*") N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	64
S1	TX ("healthy start*" OR healthystart* OR "welfare food* scheme*")	0

15. Database: CINAHL (Cumulative Index of Nursing and Allied Health Literature)

Database name	**CINAHL**
Database host	EBSCO
Database coverage dates	1983-2014
Searcher	Hannah Wood
Search date	01/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	598
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	598 (383 to main Library, 215 direct to Duplicate Library)
Reference numbers of records in EndNote library	3076-3458
Number of records after de-duplication in EndNote library	298

S61 S7 OR S59 Limiters - Published Date: 20000101-20141231 598

S60 S7 OR S59 652

S59 S28 AND S47 AND S58 231

S58 S53 NOT S57 168,757

S57 S54 OR S55 OR S56 3,937

S56 TI(metabolic N1 cost) OR AB(metabolic N1 cost) 151

S55 AB((energy or oxygen) N1 (expenditure or cost)) 2,983

S54 TI((energy or oxygen) N1 (expenditure or cost)) 1,652

S53 S48 OR S49 OR S50 OR S51 OR S52 169,615

S52 TI(budget*) OR AB(budget*) 6,622

S51 TI("value for money") OR AB("value for money") 431

S50 TI(expenditure* not energy) OR AB(expenditure* not energy) 5,016

S49 TI(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*) OR AB(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*) 106,782

S48 (MH "Economics") OR (MH "Costs and Cost Analysis+") OR (MH "Economic Aspects of Illness") OR (MH "Economic Value of Life") OR (MH "Economics, Dental") OR (MH "Economics, Pharmaceutical") OR (MH "Fees and Charges+") 93,811

S47 S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 721,015

S46 AB(child* or infant* or infancy or toddler* or neonate* or neonatal* or “neo nat*” or baby or babies or preschool* or “pre school*” or pediatric* or paediatric* or newborn* or “new born*” or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or “health visitor*” or fetal or foetus* or fetus*) 173,758

S45 TI(child* or infant* or infancy or toddler* or neonate* or neonatal* or “neo nat*” or baby or babies or preschool* or “pre school*” or pediatric* or paediatric* or newborn* or “new born*” or kindergarten* or nursery or nurseries or surestart or "sure start" or midwife* or midwives or midwifery or “health visitor*” or fetal or foetus* or fetus*) 228,681

S44 (MH "Fetal Development") 3,777

S43 (MH "Neural Tube Defects+") 3,564

S42 (MH "Fetal Abnormalities") 449

S41 (MH "Child Nutrition Disorders+") 1,208

S40 (MH "Child Health Services") 5,675

S39 (MH "Child Welfare") OR (MH "Child Behavior+") 20,561

S38 (MH "Pediatrics+") 11,784

S37 (MH "Child") OR (MH "Child, Preschool") OR (MH "Infant+") 408,684

S36 AB(mother* OR mum OR mums OR maternal* OR maternity OR childbear* OR birth* OR pregnant OR pregnanc* OR breastfeed* OR “breast feed*” OR breastfed* OR “breast fed*” OR lactating OR lactation OR conception OR periconcept* OR preconcept* OR gestation* OR pregestation* OR perigestation* OR prenatal* OR “pre natal*” OR perinatal* OR “peri natal*” OR antenatal* OR “ante natal*” OR postpartum OR “post partum” OR postnatal* OR “post natal*” OR puerperium OR puerperal OR parent OR parents OR parental OR family OR families OR caregiver* OR “care giver*” OR ((plan* OR try* OR attempt*) N2 conceive)) 196,597

S35 TI(mother* OR mum OR mums OR maternal* OR maternity OR childbear* OR birth* OR pregnant OR pregnanc* OR breastfeed* OR “breast feed*” OR breastfed* OR “breast fed*” OR lactating OR lactation OR conception OR periconcept* OR preconcept* OR gestation* OR pregestation* OR perigestation* OR prenatal* OR “pre natal*” OR perinatal* OR “peri natal*” OR antenatal* OR “ante natal*” OR postpartum OR “post partum” OR postnatal* OR “post natal*” OR puerperium OR puerperal OR parent OR parents OR parental OR family OR families OR caregiver* OR “care giver*” OR ((plan* OR try* OR attempt*) N2 conceive)) 177,536

S34 (MH "Infant Nutrition+") 16,455

S33 (MH "Pregnancy Outcomes") 12,617

S32 (MH "Mothers+") 21,703

S31 (MH "Pregnancy") OR (MH "Pregnancy, Unplanned") OR (MH "Pregnancy, Unwanted") OR (MH "Pregnancy Trimesters+") OR (MH "Prenatal Nutritional Physiology") OR (MH "Postnatal Period+") OR (MH "Periconceptual Period") 122,792

S30 (MH "Maternal Health Services+") 17,374

S29 (MH "Maternal-Child Welfare") OR (MH "Maternal Welfare") OR (MH "Maternal Behavior") OR (MH "Maternal-Child Nursing+") OR (MH "Maternal-Child Care") 27,595

S28 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 OR S26 OR S27 45,001

S27 (MH "Vitamin A") OR (MH "Vitamin A Deficiency/PC") 2,306

S26 (MH "Folic Acid+") OR (MH "Folic Acid Deficiency/PC") 5,537

S25	(MH "Ascorbic Acid") OR (MH "Ascorbic Acid Deficiency+/PC")	3,677
S24	(MH "Vitamin D+") OR (MH "Vitamin D Deficiency+/PC")	9,825
S23	AB((vitaminA* OR "retinoic acid" OR retinol OR retinoids OR retinyl OR dehydroretinol OR "aquasol A") N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	62
S22	TI((vitaminA* OR "retinoic acid" OR retinol OR retinoids OR retinyl OR dehydroretinol OR "aquasol A") N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	30
S21	AB((vitaminB* OR "folic acid" OR "folinic acid" OR folate OR folacin* OR folvite OR "pteroylglutamic acid" OR “pteroyl l glutam* acid” OR pteroylmonoglutam* OR pteroylpolyglutamat* OR methyltetrahydrofolate OR dihydrofolate OR methylfolate OR tetrahydrofolate) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	625
S20	TI((vitaminB* OR "folic acid" OR "folinic acid" OR folate OR folacin* OR folvite OR "pteroylglutamic acid" OR “pteroyl l glutam* acid” OR pteroylmonoglutam* OR pteroylpolyglutamat* OR methyltetrahydrofolate OR dihydrofolate OR methylfolate OR tetrahydrofolate) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	430
S19	AB((vitaminC* OR ascorbic* OR ascorbate OR magnorbin OR hybrin) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	47
S18	TI((vitaminC* OR ascorbic* OR ascorbate OR magnorbin OR hybrin) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	17
S17	AB((vitaminD* OR cholecalciferol* OR colecalciferol* OR ergocalciferol* OR calciferol* OR alfacalcidol*) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	37
S16	TI((vitaminD* OR cholecalciferol* OR colecalciferol* OR ergocalciferol* OR calciferol* OR alfacalcidol*) N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	32
S15	TI((wellwoman* OR "well woman*") AND (vitamin* OR supplement*)) OR AB((wellwoman* OR "well woman*") AND (vitamin* OR supplement*))	1

S14	TI(pregnacare* OR sanatogen* OR centrum* OR "seven seas" OR sevenseas* OR pharmaton* OR vitabiotic* OR abidec*) OR AB(pregnacare* OR sanatogen* OR centrum* OR "seven seas" OR sevenseas* OR pharmaton* OR vitabiotic* OR abidec*)	71
S13	TI(vitamin* OR multivitamin* OR "multi-micronutrient*" OR multimicronutrient* OR "multi-mineral*" OR multimineral* OR "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*" OR supplement OR supplements OR supplementation)	23,259
S12	AB((supplement OR supplements OR supplementation) N5 (provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	230
S11	AB((vitamin* OR multivitamin* OR "multi-micronutrient*" OR multimicronutrient* OR "multi-mineral*" OR multimineral* OR "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*") N5 (supplement* OR provision OR distribut* OR free* OR universal* OR "means-test*" OR "income dependent*" OR target* OR voucher* OR coupon* OR subsidy OR subsidies OR subsidis* OR subsidiz* OR discount*))	2,760
S10	(MH "Food Assistance")	122
S9	(MH "Dietary Supplements)	12,910
S8	(MH "Vitamins")	5,521
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6	436
S6	(MH "Vitamin A/EC/SD")	8
S5	(MH "Folic Acid+/EC/SD")	22
S4	(MH "Ascorbic Acid/EC/SD")	1
S3	(MH "Vitamin D+/EC/SD")	25
S2	(MH "Dietary Supplements/EC/SD") OR (MH "Vitamins/EC/SD")	192
S1	TI("healthy start*" OR healthystart* OR "welfare food* scheme*") OR AB("healthy start*" OR healthystart* OR "welfare food* scheme*")	194

16. Resource: NICE webpages http://www.nice.org.uk/

Database name	NICE webpages
Database host	http://www.nice.org.uk/
Database coverage dates	N/A Webpage last updated 2014
Searcher	Hannah Wood
Search date	09/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	15
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	15 (15 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	3511-3525
Number of records after de-duplication in EndNote library	

Browse: Public health guidelines: http://www.nice.org.uk/guidance/published?type=ph

Browse: Lifestyle and wellbeing: Diet, nutrition and obesity http://www.nice.org.uk/guidance/lifestyle-and-wellbeing/diet--nutrition-and-obesity

Site-wide search for the following terms:

"Healthy Start"
Vitamin
Vitamins
Multivitamin
Multivitamins
Multi-vitamin
Multi-vitamins
"Folic acid"

All results scanned by an information specialist. Choice of items to view and selection for further consideration was based on the searcher's judgment. Only those that were judged to be potentially relevant and not duplicate records were added to EndNote.

17. Resource: Public Health Observatories Webpages http://www.apho.org.uk/

Database name	Public Health Observatories Webpages
Database host	http://www.apho.org.uk/
Database coverage dates	Up to April 2013 when PHO became part of Public Health England. Webpage archived and no longer updated
Searcher	Hannah Wood
Search date	09/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	9
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	9 (9 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	3526-3534
Number of records after de-duplication in EndNote library	9

Browsed “Publications”, “Tools & Data” and “Work Streams” sections of the webpages.

Searched using “Advanced search” function. Limit 1994-2014. Note that search engine finds any occurrence of term, even within words, making truncation unnecessary. Vitamin will find vitamins, multivitamins etc. No Boolean OR available.

Any Words: Vitamin
Exact Phrase: Healthy Start
Exact Phrase: Folic acid

Filter Search By: Report

Returned results of each search were scanned for potentially relevant items. Choice of items to view and selection for further consideration was based on the searchers judgement.

18. Resource: NHS Evidence https://www.evidence.nhs.uk/

Database name	NHS Evidence
Database host	https://www.evidence.nhs.uk/
Database coverage dates	Last update 2014
Searcher	Hannah Wood
Search date	09/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	13
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	13 (9 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	3535-3547
Number of records after de-duplication in EndNote library	13

("folic acid" OR folate OR vitamin* OR multivitamin* OR “multi-micronutrient*” OR multimicronutrient* OR “multi-mineral*” OR multimineral* OR “multiple micronutrient*” OR “multiple micro-nutrient*” OR “multiple mineral*”) AND (economic* OR cost*)

“healthy start” OR healthystart

NHS Evidence does not provide the functionality to undertake a sufficiently precise search (for example it is not possible to specify the field to be searched). In order to ensure the volume of records were manageable, and that the proportion of obviously irrelevant results were not overwhelming, a very pragmatic approach was taken.

For each search, the first 200 returned results were scanned for potentially relevant items. Choice of items to view and selection for further consideration was based on the searchers judgement. Records were only added to EndNote if the record had not already been found by a previous search resource.

19. Resource: Google https://www.google.co.uk/

Database name	Google
Database host	https://www.google.co.uk/
Database coverage dates	No information provided
Searcher	Hannah Wood
Search date	10/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	15
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	15 (0 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	3548-3561, 3563
Number of records after de-duplication in EndNote library	15

For each search, the first 200 'most relevant' returned results (20 pages) were scanned for potentially relevant items. Relevance ranking was determined by the Google algorithm. Choice of items to view and selection for further consideration was based on the searcher's judgement. Records were only added to EndNote if the record had not already been found by a previous search resource.

Note: when search is limited by date, Google does not provide information on the number of records returned.

Advanced search options: http://www.google.com/advanced_search

This exact word or phrase: healthy start
Any of these words: multivitamins OR vitamins OR supplements
Site or domain: .gov.uk
File type: .pdf

This exact word or phrase: healthy start
Any of these words: multivitamins OR vitamins OR supplements
Site or domain: .nhs.uk
File type: .pdf

This exact word or phrase: healthy start
Terms appearing: in the title of the page
Site or domain: .gov.uk
File type: .pdf

This exact word or phrase: healthy start
Terms appearing: in the title of the page
Site or domain: .nhs.uk
File type: .pdf

All searches limited from 2000-2014 using the Search Tools option.

20. Database: DOPHER

Database name	**Database of promoting health effectiveness reviews (DoPHER)**
Database host	EPPI Centre Database (https://eppi.ioe.ac.uk/webdatabases/Intro.aspx?ID=2)
Database coverage dates	Information not found. States “Since January 2006 DoPHER is updated quarterly to keep it as current as possible.”
Searcher	Hannah Wood
Search date	10/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	10
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	0 (0 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	N/A
Number of records after de-duplication in EndNote library	0

No export options – records screened in database to remove obviously irrelevant records. Records only added to EndNote if the record had not already been found by a previous search resource.

1 Freetext: "healthy start" OR "healthystart" 0
2 Freetext: "economic*" OR "cost*" 613
3 Freetext: "folic acid" OR "folate" OR "vitamin*" OR "multivitamin*" 34
4 Freetext: "multi-micronutrient*" OR "multimicronutrient*" OR "multi-mineral*" OR "multimineral*" 1
5 Freetext: "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*" 1
6 3 OR 4 OR 5 34
7 2 AND 6 10
8 1 OR 7 10

0 records added to EndNote – all potentially relevant records previously identified

21. Database: TROPHI

Database name	Database of promoting health effectiveness reviews (DoPHER)
Database host	EPPI Centre Database (https://eppi.ioe.ac.uk/webdatabases/Intro.aspx?ID=2)
Database coverage dates	Information not found. States: “Quarterly sensitive searches since August 2004”
Searcher	Hannah Wood
Search date	10/10/14
Search strategy checked by	Mick Arber (information specialist YHEC)
Number of records retrieved	20
Name of EndNote library	Healthy Start.enl
Number of records loaded into EndNote	0 (0 to main Library, 0 direct to Duplicate Library)
Reference numbers of records in EndNote library	N/A
Number of records after de-duplication in EndNote library	0

No export options – records screened in database to remove obviously irrelevant records. Records only added to EndNote if the record had not already been found by a previous search resource.

1 Freetext: "healthy start" OR "healthystart" 6
2 Freetext: "economic*" OR "cost*" 679
3 Freetext: "folic acid" OR "folate" OR "vitamin*" OR "multivitamin*" 88
4 Freetext: "multi-micronutrient*" OR "multimicronutrient*" OR "multi-mineral*" OR "multimineral*" 1
5 Freetext: "multiple micronutrient*" OR "multiple micro-nutrient*" OR "multiple mineral*" 1
6 3 OR 4 OR 5 88
7 2 AND 6 14
8 1 OR 7 20

0 records added to EndNote – all potentially relevant records previously identified

22. Contacting experts

All known Healthy Start Leads (using a mailing list provided by the NHS Business Services Authority as the request of the DH to NICE) were contacted by email to request any additional evidence, particularly any grey literature or data to inform the economic model aspect of the project.

The initial email was sent on 25/09/14, with reminder emails sent to non-responders on 06/10/14 and 16/10/14. If an "out of office" or other automated reply was received which suggested an alternative contact, then a message was sent to this alternative address.

539 individuals were emailed. 106 of the email addresses were inactive or belonged to someone on long term leave (maternity, sabbatical etc.). We received 87 responses; including those from individuals who simply stated they did not work on Healthy Start, or did not hold any useful information. 21 of the responders were not on the mailing list provided, but had been forwarded the call for evidence for a colleague. **We received 36 unique documents from responders representing 13 organisations.**

The email was additionally sent to the Expert Reference Group for this project; this was managed by NICE. This approach did not result in the identification of any additional studies.

Text of call for evidence email:

RE: NICE Healthy Start Project - Request for Evidence

Good afternoon,

I am contacting you in relation to your work on Healthy Start. Your name and email address were provided to us by the Department of Health; if you are no longer working on Healthy Start we would be grateful if you could forward this email to a relevant colleague.

The York Health Economic Consortium (YHEC) are currently undertaking a systematic review and economic model to examine the cost-effectiveness of moving the Healthy Start Vitamin Programme from the current targeted offering, to a universal offering. This work has been commissioned by the National Institute for Health and Care Excellence (NICE).

Given your knowledge and expertise in this area as a Healthy Start Lead, we would be very grateful for your input into this work. This input would be appreciated in two key areas:

1) Providing us with any data or evidence on Healthy Start that may contribute to either the review or the economic model. We are particularly interested in any evidence we would be unlikely to identify through a search of databases (for example evaluations of Healthy Start that have been conducted at local level and are unpublished). We are interested in a broad range of information and outcomes including local process and evaluation reports, measures of service reach and finance reports, alongside more traditional quantitative and qualitative evidence.

2) Any information about the cost of delivering Healthy Start (either targeted provision (income assessed) or with universal provision). Any information submitted can be considered in confidence.

If you think you may be able to provide us with this information we would be grateful if you could reply to this email. We would suggest booking a brief phone call to discuss the information we need and to talk through a costing template that we would like you to complete.

Unfortunately the timescales are very short, and so we would ask you ideally to respond by Wednesday 8 October 2014.

Please do get in touch if you have any questions or would like to discuss this project further.

Many thanks,

Hannah

APPENDIX C

Excluded Studies List

Reference	Exclusion reason
Harvey, N. C., Holroyd, C., Ntani, G., Javaid, K., Cooper, P., Moon, R., Cole, Z., Tinati, T., Godfrey, K., Dennison, E., Bishop, N. J., Baird, J., Cooper, C. 2014. Vitamin D supplementation in pregnancy: a systematic review. Health Technology Assessment (Winchester, England), Vol. 18, Issue 45, pp. 1-190.	No relevant outcomes.
Power, R., 'Is Healthy Start working? Not by a long means'. 2014. Journal of Family Health Care, Vol. 24, Issue 4, pp. 30-33.	No relevant outcomes
Swaney, P., Thorp, J., Allen, I. Vitamin C supplementation in pregnancy--does it decrease rates of preterm birth? A systematic review. 2014. American Journal of Perinatology. Vol. 31, Issue 2, pp. 91-98.	No relevant outcomes
Hoeft, B., Weber, P., Eggersdorfer, M. Micronutrients - a global perspective on intake, health benefits and economics. 2012. International Journal for Vitamin & Nutrition Research, Vol. 82, Issue 5, pp. 316-320.	No relevant outcomes
Christesen, H. T., Elvander, C., Lamont, R. F., Jorgensen, J. S. The impact of vitamin D in pregnancy on extraskeletal health in children: a systematic review. 2012. Acta Obstetricia et Gynecologica Scandinavica, Vol. 91, Issue 12, pp. 1368-80.	No relevant outcomes
Moy, R. J., McGee, E., Debelle, G. D., Mather, I., Shaw, N. J. Successful public health action to reduce the incidence of symptomatic vitamin D deficiency. 2012. Archives of Disease in Childhood, Vol. 97, Issue 11, pp. 952-54.	No relevant outcomes
Yi, Y., Lindemann, M., Collings, A., Snowball, C. Economic burden of neural tube defects and impact of prevention with folic acid: a literature review. 2011. European Journal of Pediatrics, Vol. 170, Issue 11, pp. 1391-1400.	Burden of illness study
Collins, N., Friedrich, L. Multivitamin supplements--magic bullet or waste of money? 2010. Ostomy Wound Management, Vol. 56, Issue 5, pp. 18-24.	No relevant outcomes
Mouratidou, T., Ford, F. A., Wademan, S. E., Fraser, R. B. Are the benefits of the 'Healthy Start' food support scheme sustained at three months postpartum? Results from the Sheffield 'before and after' study. 2010. Maternal and Child Nutrition, Vol. 6, Issue 4, pp. 347-57.	No relevant outcomes
Greenough, A., Shaheen, S. O., Shennan, A., Seed, P. T., Poston, L. Respiratory outcomes in early childhood following antenatal vitamin C and E supplementation. 2010. Thorax, Vol. 65, Issue 11, pp. 998-1003.	No relevant outcomes
Dalziel K., Segal L., Katz R. Cost-effectiveness of mandatory folate fortification v. other options for the prevention of neural tube defects: results from Australia and New Zealand. 2010. Public Health Nutrition, Vol. 13, Issue 4, pp. 566-78.	Wrong population
Julvez, J., Fortuny, J., Mendez, M., Torrent, M., Ribas-Fito, N., Sunyer, J. Maternal use of folic acid supplements during pregnancy and four-year-old neurodevelopment in a population-based birth cohort. 2009. Paediatric and Perinatal Epidemiology, Vol. 23, Issue 3, pp. 199-206.	No relevant outcomes
Ramakrishnan, U., Nguyen, P., Martorell, R. 2009. Effects of micronutrients on growth of children under 5 y of age: meta-analyses of single and multiple nutrient interventions. 2009. American Journal of Clinical Nutrition, Vol. 89, Issue 1, pp. 191-203.	No relevant outcomes
Grosse, S. D., Ouyang, L., Collins, J. S., Green, D., Dean, J. H., Stevenson, R. E. Economic evaluation of a neural tube defect recurrence-prevention program. 2008. American Journal of Preventive Medicine, Vol. 35, Issue 6, pp. 572-77.	Wrong population
Stockley, L., Lund, V. Use of folic acid supplements, particularly by low-income and young women: a series of systematic reviews to inform public health policy in the UK. 2008. Public Health Nutrition, Vol. 11, Issue 8, pp. 807-21.	No relevant outcomes

Reference	Exclusion reason
Wilson, R. D., Johnson, J. A., Wyatt, P., Allen, V., Gagnon, A., Langlois, S., Blight, C., Audibert, F., Desilets, V., Brock, J. A., Koren, G., Goh, Y. I., Nguyen, P., Kapur, B. Genetics Committee of the Society of Obstetricians, Gynaecologists of, Canada, The Motherrisk, Program. Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies 2007. Journal of Obstetrics & Gynaecology Canada: JOGC, Vol. 29, Issue 12, pp. 1003-26.	No relevant outcomes
Neidecker-Gonzales, O., Nestel, P., Bouis, H. Estimating the global costs of vitamin A capsule supplementation: a review of the literature. 2007. Food & Nutrition Bulletin, Vol. 28, Issue 3, pp. 307-16.	No relevant outcomes
de Weerd, S., Polder, J. J., Cohen-Overbeek, T. E., Zimmermann, L. J., Steegers, E. A. Preconception care: preliminary estimates of costs and effects of smoking cessation and folic acid supplementation. 2004. Journal of Reproductive Medicine, Vol. 49, Issue 5, pp. 338-44.	Intervention not relevant
Wilson, R. D., Davies, G., Desilets, V., Reid, G. J., Summers, A., Wyatt, P., Young, D., Genetics Committee Executive, Council of the Society of Obstetricians, Gynaecologists of, Canada. The use of folic acid for the prevention of neural tube defects and other congenital anomalies. 2003. Journal of Obstetrics & Gynaecology Canada: JOGC, Vol. 25, Issue 11, pp. 959-73.	No relevant outcomes
Sircar, B. K., Ghosh, S., Sengupta, P. G., Gupta, D. N., Mondal, S. K., Sur, D., Deb, M., Manna, B., Bhattacharya, S. K. Impact of vitamin A supplementation to rural children on morbidity due to diarrhea. 2001. Indian Journal of Medical Research, Vol. 113, pp. 53-59.	Non - OECD
Vinutha, B., Mehta, M. N., Shanbag, P. Vitamin a status of pregnant women and effect of postpartum vitamin a supplementation. 2000. Indian Pediatrics, Vol. 37, Issue 11, pp. 1188-93.	Non - OECD
Sayers, A., Lawlor, D., Fraser, W. Tobias, J. H. Negligible influence of vitamin d status on cortical bone development in childhood: Findings from a large prospective cohort study. 2011. Journal of Bone and Mineral Research, Vol. 26.	Not retrievable
Metayer, C., Milne, E., Dockerty, J. D., Clavel, J., Pombo-de-Oliveira, M. S., Wesseling, C., Spector, L. G., Schuz, J., Petridou, E., Ezzat, S., Armstrong, B. K., Rudant, J., Koifman, S., Kaatsch, P., Moschovi, M., Rashed, W., Selvin, S., McCauley, K., Kang, A. Y., Hung, R. J., Buffler, P. A., Infante-Rivard, C. Maternal supplementation with folic acid and other vitamins before and during pregnancy and risk of leukemia in the offspring: A childhood leukemia international consortium (CLIC) study. 2013. Cancer Research, Vol. 73, Issue 8.	No relevant outcomes
Desai, A. M., Goebel, J. W., Cavanaugh, T. M. A cost-effectiveness analysis of vitamin d testing and supplementation strategies on quality-adjusted life-years in pediatric renal transplant recipients. 2013. Value in Health, Vol. 16, Issue 3.	Wrong population
Pentieva, K., McGarel, C., McNulty, B., Ward, M., Elliott, N., Strain, J. J.,Rollins, M. D., McNulty, H. Effect of folic acid supplementation during pregnancy on growth and cognitive development of the offspring: A pilot follow-up investigation of children of FASSTT study participants. 2012. Proceedings of the Nutrition Society, Vol. 71, Issue OCE2.	No relevant outcomes
Honest, H., Forbes, C. A., Duree, K. H., Norman, G., Duffy, S. B., Tsourapas, A., Roberts, T. E., Barton, P. M., Jowett, S. M., Hyde, C. J., Khan, K. S. Screening to prevent spontaneous preterm birth: Systematic reviews of accuracy and effectiveness literature with economic modelling. 2009. Health Technology Assessment, Vol. 13, Issue 43, pp. 1-627.	No relevant intervention

Reference	Exclusion reason
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Alm, B., Wennergren, G., Norvenius, S. G., Skjaerven, R., Lagercrantz, H., Helweg-Larsen, K., Irgens, L. M. Nordic Epidemiological Sids Study. Vitamin A and sudden infant death syndrome in Scandinavia 1992-1995. 2003. Acta Paediatrica, International Journal of Paediatrics, Vol. 92, Issue 2, pp. 162-164.	No relevant outcomes
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Shah, P. S., Ohlsoon, A. Effects of prenatal multimicronutrient supplementation on pregnancy outcomes: a meta-analysis (Structured abstract). 2009. CMAJ: Canadian Medical Association Journal, Vol. 180, Issue 12.	No relevant outcomes
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Blencowe, H., Cousens, S., Modell, B., Lawn, J. Folic acid to reduce neonatal mortality from neural tube disorders (Structured abstract). 2010. International Journal of Epidemiology, Vol. 39, Supplement 1.	No relevant outcomes
Zipitis, C. S., Akobeng, A. K. Vitamin D supplementation in early childhood and risk of type 1 diabetes: a systematic review and meta-analysis (Structured abstract). 2008. Archives of Disease in Childhood, Vol. 93, Issue 6, pp. 512-17.	No relevant outcomes
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Botto, L. D, Olney, R. S, Erickson, J. D.Vitamin supplements and the risk for congenital anomalies other than neural tube defects (Structured abstract). 2004. American Journal of Medical Genetics Part C - Seminars in Medical Genetics, Vol. 125, Issue 1, pp. 12-21.	No relevant outcomes
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Reference	Exclusion reason
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Maglione, M., Geotz, M., Wang, Z., Wagner, G., Hilton, L., Carter, J., Tringale, C., Newberry, S., Shekelle, P. Effectiveness and safety of vitamin D in relation to bone health (Structured abstract). 2007. Health Technology Assessment Database, Issue 3, p. 343.	No relevant outcomes
Chung, M., Balk, E. M., Brendel, M., Ip, S., Lau, J., Lee, J., Lichtenstein, A., Patel, K., Raman, G., Tatsioni, A., Terasawa, T., Trikalinos, T. A. Vitamin D and calcium: a systematic review of health outcomes (Structured abstract). 2009. Health Technology Assessment Database, Issue 3.	No relevant outcomes
Bond, S. Vitamins C and E Do Not Help Prevent Preeclampsia. 2008. Journal of Midwifery & Women's Health, Vol. 53, Issue 2, p. 169.	No relevant outcomes
Briley, A., Chappell, L., Kelly, F., Shennan, A., Poston, L. The Vitamins in Pre-eclampsia Study. 2001. RCM Midwives Journal, Vol. 4, Issue 9, pp. 288-291.	No relevant outcomes
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Cater. S. Healthy Start and Vitamin D Insight Project Report. 2011.	No relevant outcomes
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Nicholls, H. Cardiff Vitamin Project: Performance Evaluation Report 1st October 2011-30st September 2012. 2013.	No relevant outcomes
Tavistock Institute, Symbia. Healthy Start: Rapid Evaluation Of Early Impact On Beneficiaries, Health Professionals, Retailers And Contractors. 2012.	No relevant outcomes
Radford, J. sm Borough Council – Report To Members: The Case for additional targeted Healthy Start vitamin supplementation. 2012.	No relevant outcomes
Ellis, N. Evaluation of Camden Healthy Start vitamins pilot programme. 2014.	No relevant outcomes
Ellis, N., Patel, L. Evaluation of Islington Healthy Start vitamins pilot programme. 2014.	No relevant outcomes
Dugdall, N. Healthy Start vitamins distribution case study: Torbay. 2011.	No relevant outcomes

Reference	Exclusion reason
NHS Wales. Cardiff Vitamin Project: Performance Evaluation Report 1st April 2010-31st March 2011. 2011.	No relevant outcomes
National Institute for Health and Care Excellence. Vitamin D: implementation of existing guidance to prevent deficiency. 2014.	Not relevant in its entirety. Relevant studies already checked.
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Rotherham Borough Council. Rotherham Borough Council – Report To Members: Vitamin D. 2012.	No relevant outcomes
London Borough of Hammersmith & Fulham and O. Oyebode. Healthy start and vitamin d supplementation of mothers and children 0-5 years of age: Report of the Cabinet Member for Health and Adult Social Care. 2014.	No relevant outcomes
Whitworth, D., Dowswell, T. Routine pre-pregnancy health promotion for improving pregnancy outcomes. 2009. Cochrane System Review, Issue 4.	No relevant outcomes
EuroCat. Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe. 2009.	No relevant outcomes
Rumbold, A., Middleton, P., Pan, N., and Crowther, C. A. Vitamin supplementation for preventing miscarriage. 2011. Cochrane Database System Review, Issue 1.	No relevant outcomes
van den Broek, N., Dou, L., Othman, M., Neilson, J. P., Gates, S., Gulmezoglu, A. M. Vitamin A supplementation during pregnancy for maternal and newborn outcomes. 2010. Cochrane Database System Review, Issue 11.	No relevant outcomes
Pena-Rosas, J. P., De-Regil, L. M., Dowswell, T., Viteri, F. E. Daily oral iron supplementation during pregnancy. 2012. Cochrane Database System Review, Vol. 12.	No relevant outcomes
Lassi, Z. S., Salam, R. A., Haider, B. A., Bhutta, Z. A. Folic acid supplementation during pregnancy for maternal health and pregnancy outcomes. 2013. Cochrane Database System Review, Vol. 3.	No relevant outcomes
De-Regil, L. M., Fernandez-Gaxiola, A. C., Dowswell, T., Pena-Rosas, J. P. Effects and safety of periconceptional folate supplementation for preventing birth defects. 2010. Cochrane Database System Review, Issue 10.	No relevant outcomes
Morgan, A., Varely, D., Arber, M., Cikalo, M. Burley, Victoria J., Fitzgerald, A., Glanville, J. Vitamin D: A Systematic Review of Effectiveness and Cost-Effectiveness of Activities to Increase Awareness, Uptake and Provision of Vitamin D Supplements in at Risk Groups. 2013.	Not relevant in its entirety. Relevant studies already checked.
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Jacklin, P., Restsa, P., Kwan, I. Rapid Economic Review of Public Health Interventions Designed to Improve the Nutrition of Pre-conceptual, Pregnant and Post-Partum Women. 2006.	Wrong interventions
SHM. Maternal and Child Nutrition Programme Guidance: Fieldwork report Final version (v3.0). 2007.	No relevant outcomes
Kwan, I., Sekhri, A. Review 7: The effectiveness and cost-effectiveness of interventions to promote an optimal intake of Vitamin D to improve the nutrition of pre-conceptual, pregnant and postpartum women and children, in low income households. 2007.	No relevant outcomes
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McCormick, F., Moreton, J. A., d'Souza, D., King, S. E.,McFadden, A., Renfrew, M. J. Review 5: The effectiveness of public health interventions to improve the nutrition of young children aged 6-24 months. 2007	No relevant outcomes

Reference	Exclusion reason
D'Souza, D., King, S., McFadden, A., Moreton, J. A., Wright, K., McCormick, F., Renfrew, M. J., Dyson, L. Review 2: The effectiveness of public health interventions to improve the nutrition of pregnant women. 2007.	Wrong interventions
Kwan, I., Sekhri, A. Review 8: Supplementary review of the evidence of the effectiveness of public health interventions to improve the nutrition of infants/children aged 6 months to 5 years. 2007.	No relevant outcomes
McCormick, F., Moreton, J. A., King, S., D'Souza, L., Renfrew, M. J. Review 3: The effectiveness of public health interventions to improve the nutrition of postpartum women. 2007.	No relevant outcomes
McCormick, F., Moreton, J. A., King, S., D'Souza, L., Renfrew, M. J. Review 1: The effectiveness of public health interventions to promote nutrition of pre-conceptional women. 2007.	No relevant outcomes
National Institute for Health and Care Excellence. Costing statement: Maternal and child nutrition. 2008.	No relevant outcomes
National Institute for Health and Care Excellence. Maternal and child nutrition. 2008.	Wrong interventions
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NHS Lambeth CCG and Boots the Chemist. Agreement For Provision Of A Vitamin D Healthy Start Service By Pharmacists In Community Pharmacy Premises Within Lambeth. 2014.	No relevant outcomes
Roberts, H. Process evaluation of a new scheme offering free vitamins to families in Hackney and the City. 2012.	No relevant outcomes
Leven, L. V., Longbottom, K., Jackson A. D. Efficacy of vitamin D deficiency prevention strategies in Glasgow's maternity services. 2012. Archives of Diseases in Childhood, Vol. 97, Issue 3, p. 299.	No relevant outcomes
Jagatia, S., Lee, D., Haynes, C., Knuckey S., Cook, G. Measuring and improving vitamin D promotion and prescribing to prenatal and postnatal women within the North West. 2011.	No relevant outcomes
Austin, F., Jewell, R., Dunn, S. Healthy Start and Vitamin D Evaluation Report: Newham. 2012.	No relevant outcomes
South Warwickshire Foundation Trust. Q2 Healthy Start Returns 2014.	No relevant outcomes
South Warwickshire Foundation Trust. Q1 Healthy Start Returns 2014.	No relevant outcomes
South Warwickshire Foundation Trust. HS Returns 13-14.	No relevant outcomes
Southern Health NHS Foundation Trust. Health Start Vitamin Returns Audit 2013.	No relevant outcomes
Southern Health NHS Foundation Trust. Healthy Start Vitamin Returns Quarterly Audit.	No relevant outcomes
Tayyab, S. Healthy Start Vitamins Case Study: London Borough of Tower Hamlets.	No relevant outcomes
Peace, E. Healthy Start Vitamins Case Study: Shropshire Council.	No relevant outcomes
Clack, M. Healthy Start Vitamins Case Study: London Borough of Hackney.	No relevant outcomes
Ashfield, S. Healthy Start Audit. 2012.	No relevant outcomes
Solihull Metropolitan Council. Healthy Start: Cost of HS vitamin strategy for Solihull pregnant and breastfeeding mums and eligible families. 2014.	No relevant outcomes
Solihull Metropolitan Council. Business case: Universal provision of vitamin D for all babies in Solihull aged 4 weeks to 2 years. 2014.	No relevant outcomes
Solihull Metropolitan Council. Healthy Start – Position Statement – May 2013.	No relevant outcomes
Swindon Borough Council. Vitamin D Pathway - November 2012.	No relevant outcomes
Royal Borough of Greenwich Public Health and Well-being. Healthy Start Maternity Vitamins Pilot in QEH Evaluation Report.	No relevant outcomes
Royal Borough of Greenwich Public Health and Well-being. Healthy Start Vitamins Pilot in Greenwich Children's Centres Evaluation Report.	No relevant outcomes

Reference	Exclusion reason
Segal, L., Dalziel, K., Katz, R. A Report To Fsanz Informing A Strategy For Increasing Folate Levels To Prevent Neural Tube Defects: A Cost-Effectiveness Analysis Of Options. 2007.	Wrong population
Sefton Council. York Health Economics Consortium (YHEC) Systematic Review and Economic Model on cost effectiveness of moving the Healthy Start Vitamin Programme from the current targeted offering, to a universal offering. (Commissioned by National Institute for Health & Care Excellence – NICE). SEFTON COUNCIL PUBLIC HEALTH DEPARTMENT RESPONSE.	No relevant outcomes
Punjya, S. Establishing a Framework to Assess the Cost-Effectiveness of IIPH's Folic Acid Interventions for Women of Reproductive Age. 2013.	Non- OECD
Horton, S. The economic impact of micronutrient deficiencies. Micronutrient Deficiencies during the Weaning Period and the First Years of Life. Vol. 54, pp. 187-202.	No relevant outcomes
Gyles, C. L., Lenoir-Wijnkoop, I., Carlberg, J. G., Senanayake, V., Gutierrez-Ibarluzea, I., Poley, M. J., Dubois, D., Jones, P. J. Health economics and nutrition: a review of published evidence. Nutrition Reviews. Vol. 70, Issue 12, pp. 693-708.	No relevant intervention
Alderton, S. Do we need free vitamins for all babies and young children in the UK? Nutritional Bulletin, Vol. 39, Issue 2, pp. 187-94. 2014.	No relevant outcomes
PHE West Midlands. Briefing Paper – Healthy Start. 2014.	No relevant outcomes
MRHA. Certificate of GDP Compliance of a Wholesale Distributor: Dudley Metropolitan Borough Council. 2014.	No relevant outcomes
Dudley Public Health. Q1 2013/13 All Vitamin Return Totals. 2014.	No relevant outcomes
Healthy Start. Healthy Start quarterly report England: September 2012.	No relevant outcomes
Dudley Public Health. Healthy Start - Action Plan to Increase Uptake: 2011/2012.	No relevant outcomes
Dudley Public Health. Healthy Start Vitamins - Annual Report 2011-2012.	No relevant outcomes
Mills JL, Raymond E. Effects of recent research on recommendations for periconceptional folate supplement use. Ann N Y Acad Sci. 1993;678:137-45	No relevant intervention
Romano PS, Waitzman NJ, Scheffler RM, Pi RD. Folic acid fortification of grain: an economic analysis. Am J Public Health. 1995;85(5):667-76.	No relevant intervention

APPENDIX D

Data Extraction Tables

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Authors: Bendich *et al.* **Year:** 1997 **Aim of study:** To use published risk estimates associated with vitamin supplement intake to project potential annual cost reductions in US hospitalisation charges The following data extraction reports on the folic acid component of the work only. **Type of economic analysis:** Cost analysis **Economic perspective:** Health care system (some societal) **Quality score:** Very serious limitations **Applicability:** Partially applicable	**Source population/s:** General US population. Where the focus is on folic acid the population was all pregnant women. **Setting:** Health care system **Data sources:** Published risk estimates, annual hospitalisation charges, retail prices of vitamins.	**Intervention/s description:** Vitamin supplementation with multivitamins containing folic acid. **Comparator/control/s description:** No supplementation is implied **Sample sizes:** N/A	**Outcomes:** The outcomes of the intervention were measured in terms of the costs to the health care system of NTDs considering the extra costs of providing vitamin supplementation minus the cost of avoidable hospital charges and the lifetime cost of NTDs. **Time horizon:** 1 year and lifetime cost of spina bifida **Discount rates:** N.A. **Benefits** **Costs** NR **Perspective:** Health care system and societal costs of spina bifida **Measures of uncertainty:** NR **Modelling method**: N.A.	Based on retail prices, the cost of providing multivitamins with folic acid supplementation for pregnant women costs $162 million (£104 million). The authors calculate that reducing the risk of NTDs and other conditions at the same time, could prevent hospital charges of more than $1.3 billion (£832 million) per year, which is a cost saving[8]. **Secondary analysis:** NA	**Limitations identified by author:** None **Limitations identified by review team**: No health outcomes were included. No sensitivity analyses were reported. No model structure was reported as this was as a cost analysis. **Evidence gaps:** NR **Source of funding:** Hoffmann-LaRoche Inc.
Authors: Filby *et al.*[4] **Year:** 2014	**Source population/s:** Pregnant and breastfeeding women and children under the age of 5 years in the UK	**Intervention/s description:** Universal supplementation of vitamin D to pregnant and breastfeeding	**Outcomes:** The outcomes were the number of symptomatic vitamin D deficiency cases and the total cost associated with the	**Primary analysis:** Total costs were £14,170,915 before the intervention and £18,257,057 after the	**Limitations identified by author:** The great deal of uncertainty around the estimation of several inputs.

[8] Please note that although this study included other conditions (low birth weight and cardiovascular birth defects) in the economic evaluation, these are not outcomes of interest as defined in the scope for this project..

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Aim of study: The overall aim of this project was to provide an estimate to NICE of the cost-effectiveness of interventions to increase awareness of vitamin D guidance The economic evaluation assessed the economic impact of a campaign carried out in Birmingham to promote universal uptake of vitamin D supplementation among pregnant and breastfeeding women and children under the age of 5 years **Type of economic analysis:** Cost-consequences analysis **Economic perspective:** Health care provider (local health authority) **Quality score:** Minor limitations **Applicability:** Directly applicable	**Setting:** Primary care and outpatient setting **Data sources:** Inputs for the analysis were taken from various sources such as national registries and statistics, official health authorities as well as from published studies. Some assumptions were also made. For example, the size of the eligible population was taken from the Office for National Statistics. The cost of the intervention was derived from published studies, while the cost per unit of vitamin D was supplied by the Department of Health.	women and children under the age of 5 years **Comparator/control/s description:** The comparator was no universal supplementation of vitamin D (with Healthy Start vitamins) (the epidemiological and economic situation before the proposed intervention) **Sample sizes:** the eligible population of pregnant women and breastfeeding mothers and children under the age of 5 in the UK	intervention implementation (cost of vitamin D supplementation minus saved costs of management of symptomatic vitamin D deficiency). The cost per deficiency averted was also reported separately for women and children. **Time horizon:** Might have been 1 year **Discount rates:** N.A. **Benefits** **Costs** **Perspective:** NHS **Measures of uncertainty:** Univariate sensitivity analyses **Modelling method:** A conventional cost-effectiveness modelling framework was used to calculate the expected outcomes of the intervention. Influential inputs were prevalence of vitamin D at baseline and after the intervention; uptake of vitamin D after the intervention; annual cost of supplying vitamin D and cost of treating symptomatic vitamin D deficiency.	intervention, resulting in an incremental cost of £4,086,142 for the whole eligible population. The cost per symptomatic deficiency averted was £2,506 for pregnant/breastfeeding women and £1,229 for children under 5 years. **Secondary analysis:** Increasing the baseline prevalence of symptomatic vitamin D deficiency increases the cost-savings. A key result is that the intervention is cost-saving up to an intervention cost of around £1.5 million for pregnant/breastfeeding mothers (£2.65 million in the base case), while the intervention is never cost-saving for children.	**Limitations identified by review team**: The analysis is well presented and based on valid sources. The use of QALYs as measure of benefit would have been useful. **Evidence gaps:** There is high uncertainty around some key model parameters and some assumptions were needed **Source of funding:** NICE
Authors: Salford CCG **Year:** 2013/14	**Source population/s:** Pregnant women and breastfeeding mothers (up to	**Intervention/s description:** The intervention under	**Outcomes:** The outcomes of the proposal were the costs of universal provision of	**Primary analysis:** The yearly costs of universal provision of vitamin D	**Limitations identified by author:** N.A.

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Aim of study: To assess the economic impact of universal supply of vitamin D for targeted groups (pregnant and breastfeeding women and young children) **Type of economic analysis:** Cost analysis **Economic perspective:** NHS **Quality score:** Very serious limitations **Applicability:** Partially applicable	the age of one year of the baby) and young children (up to 4 years of age), based on data from Great Manchester and Salford **Setting:** Primary care setting in Greater Manchester and Salford **Data sources:** All data on patient demographics, prevalence, prior vitamin use, medical treatment, inpatient care, outpatient visits and final outcomes and costs appear to have been obtained from official statistics and registry databases. Data on efficacy of vitamin D supplementation in reducing vitamin D deficiency were taken from results of a health campaign in Birmingham.	examination is the universal provision of vitamin D (with Healthy Start vitamins) to pregnant women and breastfeeding mothers (up to the age of one year of the baby) and young children (up to 4 years of age) **Comparator/control/s description:** No universal supply of vitamin D (current pattern of care, for example current uptake) **Sample sizes:** N.A. (full eligible population in Greater Manchester and Salford)	vitamin D supplementation and the cost savings due to a reduction of resource use associated to treatment of vitamin D deficiency consequences **Time horizon:** The time horizon is unclear but it might have been 1 year **Discount rates:** N.A. **Benefits** **Costs** **Perspective:** The perspective of the local health authorities appears to have been adopted **Measures of uncertainty:** N.A. **Modelling method**: N.A.	supplementation were £1,821,437 (£1,323,323 after reclaims from DH) in Greater Manchester and £182,144 (£132,332 after reclaims from DH in Salford. In the latter setting, namely Salford, assuming a 10% incidence reduction, the net cost of the intervention would be £121,140. If including the distribution costs, the net cost would be £152,920. **Secondary analysis:** N.A.	**Limitations identified by review team**: This proposal focuses mainly on the budget impact of the intervention and does not derive a comprehensive benefit measure of the health impact of the proposal. No measure of benefit was estimated and the study cannot be considered a full economic evaluation. Only vitamin D related treatment costs were included. The Healthy Start vitamins offer other benefits which may not have been accounted for. **Evidence gaps:** NR **Source of funding:** NR
Authors: Salford CCG (Business case) **Year:** 2014 **Aim of study:** To estimate the economic impact of universal supplementation of Healthy Start vitamins for pregnant women and until their child is 12 months old, and for all	**Source population/s:** All pregnant women, 12 months postnatal and children under age of 5 years **Setting:** Inpatient and outpatient setting in Salford **Data sources:** Data on patient demographics, prevalence, prior vitamin use, medical treatment, inpatient care, outpatient visits and final outcomes and costs	**Intervention/s description:** Universal supplementation of Healthy Start vitamins for all mothers during pregnancy and until their child is 12 months old, and for all children under 4 years old in Salford **Comparator/control/s description:** The implicit comparator was	**Outcomes:** The outcomes of the intervention were measured in terms of the costs to the health care payer considering the extra costs of universal supplementation of Healthy Start vitamins (running costs, costs of vitamins, and costs of publicity) minus the savings due to the financial (tangible) benefits (directly correlated to uptake)	**Primary analysis:** The expected net costs of the service are £73,932 for year 1, £37,063 for year 2, and £39,632 for year 3 **Secondary analysis:** The net cost in the first, second, and third year amounts, respectively, to £37,732, £36,063, and £38,632 without publicity campaign	**Limitations identified by author:** The authors identified some inherent risks in implementing the Healthy Start scheme due to the significant variance and uncertainty in uptake levels. **Limitations identified by review team**: The study has no particular limitations although it focused mainly on the

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
children under 5 years old in Salford, UK **Type of economic analysis:** Cost analysis **Economic perspective:** Health care provider **Quality score:** Very serious limitations **Applicability:** Partially applicable	were obtained from official statistics, registries, and databases in Salford and a previous report for Greater Manchester. For example, the cost reductions in vitamin D deficiency related illnesses was taken from a report for Birmingham and Lincolnshire (plus some conservative assumptions)	the current pattern of care, which is no intervention. **Sample sizes:** the eligible population of mothers during pregnancy and until their child is 12 months old, and for all children under 4 years old in Salford	**Time horizon:** 3 years **Discount rates:** N.A. **Benefits** **Costs** **Perspective:** The perspective of the local health authorities and Department of Health appears to have been adopted **Measures of uncertainty:** Various alternative scenarios were considered (with/without publicity campaign costs and at different uptake rates) **Modelling method**: N.A.	costs; £42,873, £46,053, and £52,337 if highest rate of uptake is achieved without publicity campaign costs; and £79,073, £47,053, and £53,337 if highest rate of uptake is achieved with publicity campaign costs.	financial impact (extra costs and savings) of the intervention. No measure of benefit was estimated and the study cannot be considered a full economic evaluation Only vitamin D related health outcome treatment costs were included (rickets). The Healthy Start vitamins offer other benefits which may not have been accounted for. **Evidence gaps:** NR **Source of funding:** NR
Authors: McGee **Year:** 2010 **Aim of study:** To estimate the cost of universal vitamin D supplementation for pregnant women (and up until their child is 12 months old) and children up to four years old, in Birmingham **Type of economic analysis:**	**Source population/s:** Pregnant women and those with a child of up t 12 months old. Also, children under 4 years old. **Setting:** Birmingham (3 PCTs) **Data sources:** Local data on population numbers for target groups pregnant women and children under 4 years old (source not cited); incidence of vitamin D deficiency in under-fives 2009-2010 from survey of	**Intervention/s description:** Universal vitamin supplementation of vitamin D (with Healthy Start vitamins) . Scenario 1: All pregnant women and postnatal women and children under the age of 4. Scenario 2: All pregnant and postnatal women and only those children covered under the Healthy Start scheme **Comparator/control/s**	**Outcomes:** Cost of vitamin supplementation for target groups. Cost of treating vitamin D deficiency. **Time horizon:** One year **Discount rates:** **Benefits:** N/A **Costs:** N/A **Perspective** NHS (PCT)	**Primary analysis:** Annual cost of supplying vitamins in scenario 1: 100% uptake £659,952. 10% uptake in two PCTs and 25% uptake in one PCT £102,984. 25% uptake for women and children citywide (all 3 PCTs) £164,988. Estimated cost of treated rickets for one year = £5,000 x 33 cases = £165,000.	**Limitations identified by author:** **NR** **Limitations identified by review team**: Not a formal economic evaluation but a costing study. The source of treatment cost was not reported. Only the cost of purchasing the vitamin and delivery were included. Resource use,

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Cost analysis Compared the cost of two scenarios of 'universal' supplementation. **Economic perspective:** NHS **Quality score:** Very serious limitations **Applicability:** Partially applicable	cases of children in three Birmingham PCTs treated for vitamin D deficiency; number of Healthy Start beneficiaries from DH data; local cost of Healthy Start vitamins; and costs of delivery to different distribution points. Cost of treating vitamin D deficiency estimated at £5,000 per year (source not cited).	**description:** No universal supplementation **Sample sizes:** Total: 17,311 pregnant women and 68,609 children under 4 Intervention: As above. Control: NR	**Measures of uncertainty** No uncertainty analysis was undertaken. **Modelling method** This was a costing study. The study estimated the cost of vitamin supplementation in the two target groups based on different uptake scenarios. These were compared to the cost of treating vitamin D deficiency in Birmingham.	Annual cost of supplying vitamins in scenario 2: 100% uptake £124,414. 25% uptake £31,103. **Secondary analysis:** NR.	training *etc.* were not included. Only vitamin D related treatment costs were included. The Healthy Start vitamins offer other benefits which may not have been accounted for. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR
Authors: NHS Lambeth CCG (Business case) **Year:** 2013/2014 **Aim of study:** To estimate the economic impact of universal supplementation of vitamin D for all mothers during pregnancy and until their child is 12 months old, and for all children under 4 years old in the area of Lambeth and Southwark (UK), not only to comply with recent national recommendations but also to reduce health inequalities in vitamin D deficiency	**Source population/s:** Pregnant women and breastfeeding mothers (up to the age of one year of the baby) and children up to the age of 4 years, based on data from Lambeth & Southwark **Setting:** Inpatient and outpatient setting in Lambeth & Southwark **Data sources:** All data on patient demographics, prevalence, prior vitamin use, medical treatment, inpatient care, outpatient visits and final outcomes and costs were obtained from official statistics and databases in Lambeth & Southwark. For example, outpatient data were taken from the	**Intervention/s description:** Universal supplementation of vitamin D (with Healthy Start vitamins) for all mothers during pregnancy and until their child is 12 months old, and for all children under 4 years old provided through the Healthy start vitamins **Comparator/control/s description:** Universal supplementation of vitamin D is solely for babies up to 6 months of age (current standard of care) **Sample sizes:** the eligible population of mothers during	**Outcomes:** The outcomes of the intervention were measured in terms of the costs to the health care payer considering the extra costs of universal provision of vitamin D minus the savings due to the reduced costs associated to lower incidence of vitamin D deficiency **Time horizon:** The time horizon is unclear as the proposal applies to the future policy of the local health authorities (results reported fully for the first year) **Discount rates:** N.A. **Benefits** **Costs** **Perspective:** The	**Primary analysis:** The expected costs of the intervention are £180,342 for the first year (£90,171 for Southwark and £90,171 for Lambeth) and £118,195 for subsequent years (£59,097.50 for each borough). The costs associated with vitamin D deficiency and rickets in Lambeth & Southwark which is estimated to cost £383,102 per annum (much higher than the cost of programme implementation). Hypothetical scenarios for the impact of the intervention on vitamin D deficiency and rickets	**Limitations identified by author:** N.A. **Limitations identified by review team**: This proposal focuses mainly on the budget impact of the intervention and does not derive a comprehensive benefit measure of the health impact of the proposal. It cannot be considered a full economic evaluation. Only vitamin D related costs were included. The Healthy Start vitamins offer other benefits which may not have been accounted for. **Evidence gaps:**

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Type of economic analysis: Cost analysis **Economic perspective:** Health care provider **Quality score:** Very serious limitations **Applicability:** Partially applicable	database of the Evelina Children's Hospital and the Kings College Hospital in 2012. Admission costs were based on tariff costs assigned by the Healthcare Resources Group.	pregnancy and until their child is 12 months old, and for all children under 4 years old in the two areas of Lambeth and Southwark (n=34,013)	perspective of the local health authorities appears to have been adopted **Measures of uncertainty:** N.A. **Modelling method**: N.A.	prevalence were also considered. **Secondary analysis:** N.A.	NR **Source of funding:** NR
Authors: Postma *et al.* **Year:** 2002 **Aim of study:** To estimate the cost-effectiveness of periconceptional supplementation of folic acid using pharmacoeconomic model calculation **Type of economic analysis:** Cost-effectiveness analysis **Economic perspective:** Society but only direct costs (inside and outside the health sector) are included	**Source population/s:** Dutch pregnant women and women trying to become pregnant (hypothetical population for the economic model) **Setting:** Health-care setting in the Netherlands **Data sources:** Costs of folic acid supplementation: Dutch drug price list Prevalence data: Dutch studies and registry Efficacy data: published studies Costs for spina bifida: One study carried out in the US Discounted life-years gained per prevented case of spina bifida: Assumption Life expectancy: Dutch central Bureau of Statistics	**Intervention/s description:** Folic acid supplementation (0.5mg, daily) from at least 4 weeks before until at least 8 weeks after conception. **Comparator/control/s description:** No folic acid supplementation (current pattern of care in the Dutch setting) **Sample sizes:** N/A	**Outcomes:** Model outcomes were the costs and benefits (measured as life-year gained) of the interventions, which were calculated using mainly objective data **Time horizon:** Lifetime **Discount rates:** **Benefits:** 4% **Costs:** 4% **Perspective:** Society **Measures of uncertainty:** Univariate, multivariate, and probabilistic sensitivity analysis **Modelling method**: A conventional pharmacoeconomic model with the outcome expressed in net costs per life-year gained was used	**Primary analysis:** The incremental cost per discounted life-year gained through periconceptional supplementation of acid folic was NLG 3,900 using 2000 prices. £1,488.90. **Secondary analysis:** The cost-effectiveness remained mostly below NLG 10,000 (€4,500) (£3,817.69) using plausible alternative inputs and ranged from cost-saving to a maximum of NLG 14,900 (£5,688.35) in the multivariate analysis and NLG 12,900 (£4924.82) in the probabilistic sensitivity analysis	**Limitations identified by author:** The authors acknowledged that the use of QALYs would have strengthened the analysis. Moreover, the estimate of direct costs of care for spina bifida were not available in the Netherlands and were taken from a US source, thus leading to transferability issues related to the differences between the Dutch and US health care systems. It was also stated that some assumptions made in the model were conservative and thus the economic and health benefits of the intervention might have been underestimated. **Limitations identified by review team**: The analysis is well carried out but data sources are

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
					generally not clearly described. More details on total costs and benefits of the interventions compared would have been useful (only ICERs reported). The study was published in 2002 and it may be not relevant given more recent data available to decision makers. **Evidence gaps:** Need for assumptions on total costs and survival for children with spina bifida. **Source of funding:** None
Authors: Turner *et al.* **Year:** 2012 **Aim of study:** The aim of this three month project was to investigate the potential health effects of universal access to Healthy Start vitamins with particular regard to Vitamin D on all pregnant women and breastfeeding mothers and children up to the age of 5 within Greater Manchester.	**Source population/s:** Pregnant women and breastfeeding mothers up to one year postnatally and children up to the age of 5. **Setting:** Greater Manchester **Data sources:** Costs: HS supplements: DH Treatment of vitamin D deficiency: NHS Treatment of rickets: unknown Number of live births in Greater Manchester 2011: Children's network data Number of women eligible for HS: HS DH	**Intervention/s description:** Universal supplementation (with Healthy Start vitamins) in target group **Comparator/control/s description:** Vitamin supplementation as present No comparative analysis was conducted. **Sample sizes:** N/A	**Outcomes:** Cost of vitamin supplementation Cost of treating vitamin deficiency. **Time horizon:** NR – options for 3 years are given in executive summary. **Discount rates:** **Benefits:** N/A **Costs:** No discounting **Perspective** NHS **Measures of uncertainty** No uncertainty analysis was undertaken	**Primary analysis:** Cost of supplying universally assuming 100% uptake: £2,336,475. Cost after claiming back HS costs from DH: £1,676,592 Savings from reduced spending on treatment for vitamin D deficiency: £4,248,322 Other savings could sum to £6,260,322 (reduced spending on prescribing folic acid, treatment of rickets). **Secondary analysis:** No sensitivity analysis. Scenarios reported in	**Limitations identified by author:** NR **Limitations identified by review team**: Report includes some crude estimates of costs. Cost of implementing the scheme only included the costs of supplying the vitamins, no resource use included. Estimates of cost savings were also crude and comprised of reduced costs of treating vitamin D deficiency, including blood tests and General Practitioner (GP) visits as well as treatment with vitamins. Sources for

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Type of economic analysis: Cost analysis only **Economic perspective:** NHS **Quality score:** Very serious limitations **Applicability:** Partially applicable			**Modelling method** Costs were estimated on 38,716 women who delivered 39,256 children in 2011 in Greater Manchester. 3,753 pregnant women claimed HS in 2011 and 12,330 children claimed. Assumed 100% uptake of vitamins and claim back for all HS recipients.	executive summary but not main text. 10% uptake would cost £233,648 (£167,659 if HS claimed back). 16% uptake would cost £373,836 (£268,255 is HS claimed back. 25% uptake £584,119 (£419,148 is HS claimed back). No information on savings with these uptakes.	these costs were not provided. Data in tables were not clearly presented and it was not possible to unpick the different elements of resources and unit costs from the estimation of total costs. Costs presented in the executive summary were not included in the main report (different uptake scenarios). However, the review team found it was simply a percentage of the costs in the main report. These costs were reported over 3 years in the executive summary and no discounting was applied. They also only included the cost of vitamins and the cost savings associated with different uptake levels were not reported. The report focuses on vitamin D deficiency costs, no benefits from the other vitamins supplied in HS are included. **Evidence gaps and/or recommendations for future research:** NR

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
					Source of funding: Not reported
Authors: Zipitis et al. **Year:** 2006 **Aim of study:** To verify whether vitamin D deficiency is re-emerging in the catchment area since funding of vitamin D supplementation by Primary Care Trusts ceased, and to assess the cost-effectiveness of reintroducing vitamin D supplementation in the Burnley Health Care NHS Trust. **Type of economic analysis:** Costing study (retrospective study) **Economic perspective:** Not specifically reported (Health care provider) **Quality score:** **Very serious limitations**	**Source population/s:** Vitamin D deficient paediatric patients presenting at a hospital paediatric department in Burnley, UK, between January 1994 and May 2005. Catchment area of the Burnley Health Care NHS Trust covers the boroughs of Burnley, Pendle, and Rossendale in North West England. Population about 242 000. 14 clinical cases were reviewed of which 93% were of Asian origin. **Setting:** Outpatient/inpatient care: Hospital paediatric department in Burnley, North West England, UK. **Data sources:** Data on patient demographics, prior vitamin use, investigations and treatment, inpatient care, follow-up appointments and final outcome were obtained from a review of patient records (identified through specific searches).	**Intervention/s description:** 1. Supplementation with vitamin D if DH at the time (supplementation for the firsy 5 years) recommendations were implemented in Burnley NHS Trust. 2. Supplementation with vitamin D if COMA[9] guidelines at the time (supplementation for the first 2 years) were implemented in Burnley NHS Trust. **Comparator/control/s description:** No free supplementation offered. **Sample sizes:** Total: Clinical information from 14 patients with vitamin D deficiency Intervention: N/A Control: N/A	**Outcomes:** Cost of treating vitamin D deficiency and the cost of primary prevention. **Time horizon:** 1 year **Discount rates:** **Benefits:** N/A **Costs:** N/A **Perspective** NHS Trust **Measures of uncertainty** No uncertainty analysis was carried out **Modelling method** The cost of treating vitamin D deficiency in children was collected retrospectively. Then the theoretical cost of primary prevention was calculated according the DH and COMA guidelines. The cost of preventing one case of vitamin D deficiency was calculated.	**Primary analysis:** The total cost of treating one vitamin D deficiency was £2,505 per patient. The cost of preventing one case of vitamin D deficiency in the Trust's child population was £19,014 (COMA) or £47,535 (DH). Total annual cost of primary prevention for whole Trust population was £82,400 (COMA) or £206,000 (DH) Incremental costs of supplementation versus no supplementation were increased costs of £71,542.50 or of £195,143 according to the COMA and DH guidelines, respectively (calculated by reviewers) **Secondary analysis:** No sensitivity analysis carried out.	**Limitations identified by author:** Study was retrospective. The population characteristics of the patients identified may be special in terms of low socioeconomic status, this rendering generalisation of these results problematic. **Limitations identified by review team**: Small sample size. Not all the health effects of supplementation with Abidec (a multivitamin) were considered. Not all relevant costs were included: costs of distribution, resource use and staff training etc. were not included. **Evidence gaps and/or recommendations for future research:** None identified.

[9] **The reports refers to the following COMA report: Department of Health. Department of Health Report on Health and Social Subjects. 49 Nutrition and bone health with particular reference to calcium and vitamin D. Report of the Subgroup on Bone Health, Working Group on the Nutritional Status of the Population of the Committee on Medical Aspects of Food Policy. London: HMSO, 1998.

Study details	Population and setting	Intervention / comparator	Outcomes and methods of analysis	Results	Notes by review team
Applicability: Partially applicable	Costs of investigations, hospital expenses and medication based on published sources (Trust departments and British National Formulary values). Yearly cost of multivitamins (Abidec) was an average from the published range. Trust figures and 2001 Census data also used.		This was calculated for the whole Trust population (incidence of deficiency of 1 in 923) and for the Trust's Asian population (incidence of deficiency of 1 in 117).		**Source of funding:** NR

APPENDIX E

Quality Appraisal Checklists

Quality criterion	Bendich, 1997	Filby, 2014[4]	Salford CCG, 2013	Salford CCG, 2014	McGee, 2010	NHS Lambeth, 2014	Postma, 2002	Turner, 2012	Zipitis, 2006
1.1	P	Y	Y	Y	Y	Y	Y	Y	P
1.2	Y	Y	Y	Y	Y	Y	Y	Y	Y
1.3	P	Y	Y	Y	Y	Y	P	Y	Y
1.4	N	Y	Y	Y	Y	P	Y	Y	Y
1.5	Y	P	N	N	Y	N	Y	N	Y
1.6	N	N	N	N	N.A	N	Y	N	N
1.7	N.A	N	N	N	N.A	N	N	N.A	N.A
1.8	U	N	N	N	N	N	P	N	N.A
Overall judgement	Partially applicable	Partially applicable	Partially applicable	Partially applicable	Partially applicable	Partially applicable	Partially applicable	Partially applicable	Partially applicable
2.1	N.A	P	N.A	N.A	N.A	N.A	U	N.A	N.A
2.2	P	N	N	P	P	U	Y	U	P
2.3	N	P	N.A	N.A	N	N.A	Y	N	N
2.4	N.A	P	N.A	N.A	N.A	N.A	P	N.A	N.A
2.5	Y	Y	N.A	N.A	N.A	N.A	U	N.A	N.A
2.6	N	P	P	P	N	P	P	N	N
2.7	Y	P	Y	Y	U	Y	U	U	U
2.8	Y	Y	P	U	N.A	Y	U	U	U
2.9	N	Y	N	N	N	N	Y	N	N
2.10	N	P	N	P	N	N.A	P	N	N
2.11	U	U	U	U	U	U	U	U	U
Overall assessment	Very serious limitations	Minor limitations	Very serious limitations	Very serious limitations	Very serious limitations	Very serious limitations	Potentially serious limitations	Very serious limitations	Very serious limitations

Study identification:	Bendich, A., Mallick, R, Leader, S. Potential health economic benefits of vitamin supplementation. West J Med. 1997; 166:306.		
Guidance topic:	N/A		
Checklist completed by:	Alex Filby and Scott Mahony		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1	Is the study population appropriate for the topic being evaluated??	Partly	Pregnant women
1.2	Are the interventions appropriate for the topic being evaluated??	Yes	Multivitamin containing folic acid supplementation
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Partly	US health care system
1.4	Was/were the perspective(s) clearly stated and what were they?	No	Appears to be the cost to the healthcare system with a societal cost of NTDs
1.5	Are all direct health effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are both costs and health effects discounted appropriately?	No	No discounting reported
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	N/A	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	Unclear what perspective was taken
Overall judgement: directly applicable/partially applicable/not applicable There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality) This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	N/A	Cost analysis only
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Annual costs and lifetime cost of spina bifida
2.3	Are all important and relevant health outcomes included?	No	Cost analysis only, so health outcomes are not reported

2.4	Are the estimates of baseline health outcomes from the best available source?	N/A	
2.5	Are the estimates of relative 'treatment' effects from the best available source?	Yes	
2.6	Are all important and relevant costs included?	No	Only the costs of purchasing vitamins is included
2.7	Are the estimates of resource use from the best available source?	Yes	Annual hospitalisation charges
2.8	Are the unit costs of resources from the best available source?	Yes	Annual hospitalisation charges
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	No	No sensitivity analysis, although ranges of relative risks from various studies were included
2.11	Is there any potential conflict of interest?	Unclear	
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	No resource use included, no discounting, and no sensitivity analysis
Other comments:			

Study identification:	Filby A, Lewis L, Taylor M. An Economic Evaluation of Interventions to Improve the Uptake of Vitamin D Supplements in England and Wales. YHEC; 2014.[4]		
Guidance topic:	N/A		
Checklist completed by:	Marco Barbieri and Gabriella Giunta		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1	Is the study population appropriate for the topic being evaluated??	Yes	Pregnant and breastfeeding women and children under the age of 5 years
1.2	Are the interventions appropriate for the topic being evaluated??	Yes	Vitamin D supplementation
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Conducted in the UK
1.4	Was/were the perspective(s) clearly stated and what were they?	Yes	NHS
1.5	Are all direct health effects on individuals included, and are all other effects included where they are material?	Partly	Only vitamin D deficiency estimated, not long-term effects of this deficiency
1.6	Are both costs and health effects discounted appropriately?	No	
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	No	
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	Partly	A very simple decision model was used
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	Short-term
2.3	Are all important and relevant health outcomes included?	Partly	Long-term effect of vitamin D not considered
2.4	Are the estimates of baseline health outcomes from the best available source?	Partly	Taken from studies only partially described
2.5	Are the estimates of relative 'treatment' effects from the best available source?	Yes	From real UK data
2.6	Are all important and relevant costs included?	Partly	Costs are consistent with the health care payer perspective. Long-term costs not considered
2.7	Are the estimates of resource use from the	Partly	Some sources not fully

	best available source?		described
2.8	Are the unit costs of resources from the best available source?	Yes	UK standard sources
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	However, a more generic benefit measure would have been useful
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	Partly	No probabilistic sensitivity analysis was made
2.11	Is there any potential conflict of interest?	Unclear	
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Minor limitations	
Other comments:			

Study identification:	Salford CCG. Costed Options Appraisal for Commissioning the Healthy Start Programme in Salford. 2013.		
Guidance topic:	N/A		
Checklist completed by:	Marco Barbieri and Gabriella Giunta		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1	Is the study population appropriate for the topic being evaluated??	Yes	All pregnant women, 9 months prenatal, 12 months postnatal and children under age of 4 years
1.2	Are the interventions appropriate for the topic being evaluated??	Yes	Universal supplementation of Healthy Start vitamins
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Study conducted in Greater Manchester and Salford, UK
1.4	Was/were the perspective(s) clearly stated and what were they?	Yes	Local authorities and Department of Health
1.5	Are all direct health effects on individuals included, and are all other effects included where they are material?	No	Health benefits not considered
1.6	Are both costs and health effects discounted appropriately?	No	
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	No	Health benefits not considered
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	N.A.	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	Only 1 year considered
2.3	Are all important and relevant health outcomes included?	N.A.	Not included
2.4	Are the estimates of baseline health outcomes from the best available source?	N.A.	
2.5	Are the estimates of relative 'treatment' effects from the best available source?	N.A.	
2.6	Are all important and relevant costs included?	Partly	Cost saving associated to reduce risk of future diseases not considered
2.7	Are the estimates of resource use from the	Yes	Local databases and

	best available source?		registries
2.8	Are the unit costs of resources from the best available source?	Partly	Some sources not described
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	No	Only alternative scenarios on risk reduction
2.11	Is there any potential conflict of interest?	Unclear	
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	This is not a full economic evaluation
Other comments:			

Study identification:	Salford CCG. Business Case: Healthy Start Vitamin D. 2014.		
Guidance topic:	N/A		
Checklist completed by:	Marco Barbieri and Gabriella Giunta		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1	Is the study population appropriate for the topic being evaluated??	Yes	All pregnant women, 9 months prenatal, 12 months postnatal and children under age of 4 years
1.2	Are the interventions appropriate for the topic being evaluated??	Yes	Universal supplementation of Healthy Start vitamins
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Study conducted in Salford, UK
1.4	Was/were the perspective(s) clearly stated and what were they?	Yes	Local authorities and Department of Health
1.5	Are all direct health effects on individuals included, and are all other effects included where they are material?	No	Health benefits not considered
1.6	Are both costs and health effects discounted appropriately?	No	
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	No	Health benefits not considered
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	N.A.	
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Only 3 years considered, impact of programme on cost savings might be higher in the long-term
2.3	Are all important and relevant health outcomes included?	N.A.	Not included
2.4	Are the estimates of baseline health outcomes from the best available source?	N.A.	
2.5	Are the estimates of relative 'treatment' effects from the best available source?	N.A.	
2.6	Are all important and relevant costs included?	Partly	Cost saving associated to reduce risk of future diseases not considered

2.7	Are the estimates of resource use from the best available source?	Yes	Local databases and registries
2.8	Are the unit costs of resources from the best available source?	Unclear	Not all sources described
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	Partly	Only alternative scenarios included
2.11	Is there any potential conflict of interest?	Unclear	
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	This is not a full economic evaluation
Other comments:			

Study identification:	McGee E. Prevention of rickets and vitamin D deficiency in Birmingham: The case for universal supplementation. Birmingham: National Health Service; 2010.		
Guidance topic:	N/A		
Checklist completed by:	Alex Filby and Michelle Jenks		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1 Is the study population appropriate for the topic being evaluated??		Yes	Pregnant women, post-partum for one year and children under 4 years.
1.2 Are the interventions appropriate for the topic being evaluated??		Yes	Healthy Start supplements
1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?		Yes	Birmingham
1.4 Was/were the perspective(s) clearly stated and what were they?		Yes	NHS
1.5 Are all direct health effects on individuals included, and are all other effects included where they are material?		Yes	
1.6 Are both costs and health effects discounted appropriately?		N/A	No discounting reported but time horizon only one year.
1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?		N/A	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?		No	NHS only
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?		N/A	Cost analysis only
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		Partly	One year
2.3 Are all important and relevant health outcomes included?		No	Cost analysis only, so health outcomes are not reported
2.4 Are the estimates of baseline health outcomes from the best available source?		N/A	
2.5 Are the estimates of relative 'treatment' effects from the best available source?		N/A	
2.6 Are all important and relevant costs included?		No	Only the costs of purchasing vitamins and delivery are included.
2.7 Are the estimates of resource use from the		Unclear	

	best available source?		
2.8	Are the unit costs of resources from the best available source?	N/A	Not reported. E.g. cost of treating rickets is estimated to be £5000. No source given.
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	No	No sensitivity analysis
2.11	Is there any potential conflict of interest?	Unclear	Source of funding not reported.
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	All relevant costs not included no resource use, no sensitivity analysis.
Other comments:			

Study identification:	NHS Lambeth CCG Agreement For Provision Of A Vitamin D Healthy Start Service By Pharmacists In Community Pharmacy Premises, Within Lambeth. Appendix I. 2014.
Guidance topic:	
Checklist completed by:	Marco Barbieri and Gabriella Giunta

Applicability		
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies	Yes/No/Partly/ Unclear/N.A.	Comments
1.1 Is the study population appropriate for the topic being evaluated??	Yes	Pregnant women and breastfeeding mothers (up to the age of one year of the baby) and children up to the age of 4 years
1.2 Are the interventions appropriate for the topic being evaluated??	Yes	Vitamin D supplementation (micrograms reported)
1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Conducted in the UK local authorities
1.4 Was/were the perspective(s) clearly stated and what were they?	Partly	The perspective of two local authorities was taken
1.5 Are all direct health effects on individuals included, and are all other effects included where they are material?	No	Benefits not considered
1.6 Are both costs and health effects discounted appropriately?	No	Short time horizon
1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	No	Benefits not considered
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'	Partially applicable	
Other comments:		

Quality		
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].	Yes/No/Partly/ Unclear/N.A.	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	N.A.	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Unclear	Time horizon not explicitly reported
2.3 Are all important and relevant health outcomes included?	N.A.	No benefits reported
2.4 Are the estimates of baseline health outcomes from the best available source?	N.A.	
2.5 Are the estimates of relative 'treatment' effects from the best available source?	N.A.	
2.6 Are all important and relevant costs included?	Partly	Only those related to health authorities
2.7 Are the estimates of resource use from the	Yes	Local databases and

	best available source?		registries
2.8	Are the unit costs of resources from the best available source?	Yes	
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	N.A.	
2.11	Is there any potential conflict of interest?	Unclear	
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	This is not a full economic evaluation
Other comments:			

Study identification:	Postma MJL, J. Veenstra, M. de Walle, H. E. K. de Jong-van den Berg, L. T. W. Cost-effectiveness of periconceptional supplementation of folic acid. Pharm. World Sci. 2002;24(1):8-11.
Guidance topic:	N/A
Checklist completed by:	Marco Barbieri and Gabriella Giunta

Applicability		
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies	Yes/No/Partly/ Unclear/N.A.	Comments
1.1 Is the study population appropriate for the topic being evaluated??	Yes	Pregnant women and women trying to become pregnant (no age restriction)
1.2 Are the interventions appropriate for the topic being evaluated??	Yes	Folic acid supplementation was compared with no folic acid which was the current standard in the authors' setting at the time of the study
1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Partly	Study conducted more than 10 years ago in the Netherlands
1.4 Was/were the perspective(s) clearly stated and what were they?	Yes	Societal (with exclusion of indirect costs)
1.5 Are all direct health effects on individuals included, and are all other effects included where they are material?	Yes	Life-years gained
1.6 Are both costs and health effects discounted appropriately?	Yes	Dutch guidelines
1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	No	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Partly	Productivity losses not considered
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'	Partially applicable	
Other comments:		

Quality		
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].	Yes/No/Partly/ Unclear/N.A.	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Unclear	Model not fully described
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Lifetime
2.3 Are all important and relevant health outcomes included?	Yes	
2.4 Are the estimates of baseline health outcomes from the best available source?	Partly	Prevalence of spinal bifida taken from a Dutch study not fully described and baseline risk of no acid folic implementation

		inversely calculated taking account of relative risk reduction of folic acid on overall prevalence
2.5 Are the estimates of relative 'treatment' effects from the best available source?	Unclear	Sources not described
2.6 Are all important and relevant costs included?	Partly	Productivity gains of avoiding spinal bifida not considered (conservative)
2.7 Are the estimates of resource use from the best available source?	Unclear	Resource use and unit costs not presented separately for important items
2.8 Are the unit costs of resources from the best available source?	Unclear	Resource use and unit costs not presented separately for important items
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	However, total costs and benefits not reported separately
2.10 Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	Partly	The authors stated that uncertainty in all parameters was considered but little information was given
2.11 Is there any potential conflict of interest?	Unclear	Source of funding not reported
2.12 **Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Potentially serious limitations	Need for assumptions for key model inputs (e.g. costs and survival of individuals with spinal bifida), poor description of important sources (e.g. treatment effect)
Other comments:		

Study identification:	Turner HS, C. Sachs, M. O'Conner, B. Dawson, J. Rapid Health Impact Assessment of the effects of Vitamin D for women and children in Greater Manchester Greater Manchester Public Health Network Greater Manchester Children, Young People & Family Network 2012.
Guidance topic:	N/A
Checklist completed by:	Alex Filby and Michelle Jenks

Applicability		
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies	Yes/No/Partly/ Unclear/N.A.	Comments
1.1 Is the study population appropriate for the topic being evaluated??	Yes	Pregnant women, up to 1 year postnatally and children 6 weeks – 5 years
1.2 Are the interventions appropriate for the topic being evaluated??	Yes	Healthy Start supplements
1.3 Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Greater Manchester
1.4 Was/were the perspective(s) clearly stated and what were they?	Yes	NHS
1.5 Are all direct health effects on individuals included, and are all other effects included where they are material?	No	Only rickets included
1.6 Are both costs and health effects discounted appropriately?	No	No discounting reported
1.7 Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	N/A	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	No	NHS only
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'	Partially applicable	
Other comments:		

Quality		
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].	Yes/No/Partly/ Unclear/N.A.	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	N/A	Cost analysis only.
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Unclear	Not reported
2.3 Are all important and relevant health outcomes included?	No	Cost analysis only, so health outcomes are not reported
2.4 Are the estimates of baseline health outcomes from the best available source?	N/A	
2.5 Are the estimates of relative 'treatment' effects from the best available source?	N/A	
2.6 Are all important and relevant costs included?	No	Only the cost of the vitamins is included
2.7 Are the estimates of resource use from the	Unclear	

	best available source?		
2.8	Are the unit costs of resources from the best available source?	Unclear	Not reported. E.g. cost of treating rickets is estimated to be £5000. No source given.
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	No	No sensitivity analysis reported.
2.11	Is there any potential conflict of interest?	Unclear	Source of funding not reported.
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	Not all costs included, resource use not estimated, no discounting, no sensitivity analysis, only outcome considered if rickets.
Other comments:			

Study identification:	Zipitis CSM, G. A. Swann, I. L. Vitamin D deficiency: prevention or treatment? Arch Dis Child. 2006;91(12):1011-4.		
Guidance topic:	N/A		
Checklist completed by:	Alex Filby and Michelle Jenks		
Applicability			
Section 1: Applicability (relevance to specific topic review question(s) and the NICE reference case[a]) This checklist should be used first to filter out irrelevant studies		Yes/No/Partly/ Unclear/N.A.	Comments
1.1	Is the study population appropriate for the topic being evaluated??	Partly	Children aged under 15 with vitamin D deficiency
1.2	Are the interventions appropriate for the topic being evaluated??	Yes	Vitamin D supplementation
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK context?	Yes	Burnley
1.4	Was/were the perspective(s) clearly stated and what were they?	Yes	Perspective of Burnley Health Care NHS Trust
1.5	Are all direct health effects on individuals included, and are all other effects included where they are material?	Yes	
1.6	Are both costs and health effects discounted appropriately?	No	No discounting reported
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?	N/A	
1.8	Are costs and outcomes from other sectors fully and appropriately measured and valued?	N/A	NHS Trust only
Overall judgement: directly applicable/partially applicable/not applicable. There is no need to complete section 2 of the checklist if the study is considered 'not applicable'		Partially applicable	
Other comments:			
Quality			
Section 2: Study limitations (the level of methodological quality). This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline[b].		Yes/No/Partly/ Unclear/N.A.	Comments
2.1	Does the model structure adequately reflect the nature of the topic under evaluation?	N/A	Cost analysis only
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Costs estimated over 2 and 5 years
2.3	Are all important and relevant health outcomes included?	No	Cost analysis only, so health outcomes are not reported
2.4	Are the estimates of baseline health outcomes from the best available source?	N/A	
2.5	Are the estimates of relative 'treatment' effects from the best available source?	N/A	
2.6	Are all important and relevant costs included?	No	Only the costs of purchasing vitamins is included
2.7	Are the estimates of resource use from the best available source?	Unclear	
2.8	Are the unit costs of resources from the best	Unclear	

	available source?		
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10	Are all important parameters, whose values are uncertain, subjected to appropriate sensitivity analysis?	No	No sensitivity analysis
2.11	Is there any potential conflict of interest?	Unclear	Source of funding not reported
2.12	**Overall assessment:** minor limitations/potentially serious limitations/very serious limitations	Very serious limitations	No resource use included, no discounting, and no sensitivity analysis
Other comments:			